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EVALUATION OF MATERNAL REJECTION THEORY IN ALLERGY

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RECENT controversy over the notion that allergic symptoms are intensified or even induced primarily by maternal rejection has led me to explore more carefully this point of view in terms of both the psychodynamic theory and its application to the therapy of the allergic patient. In particular, I should like to present the point of view that the psychodynamic theory of maternal rejection so often cited as the basic part of the emotional difficulty of the patient is often not only incomplete but may frequently be misleading in understanding and treating the allergic responses of children and of adults. I shall hold that on the basis of my studies the allergic child is not primarily rejected by the mother or father but that rather the opposite may occur.[1] Briefly, in certain cases where the eczema persists and no simple allergic process can be discovered, or where the intensity of the asthma progresses in uncontrollable form, the disturbance in the parent-child relationship is not parental rejection but rather mutual engulfment (introjection). This concept has been previously applied to the rôle of the mother in psychosomatic problems in general by Sperling[5] and to schizophrenia by Lidz and Lidz.[3] We may safely broaden the concept to include fathers, especially with male children. Rejection may ensue when the mutual engulfment fails to satisfy the parental needs. Then the rage of the frustrated parent may lead to rejection in a few areas but not in all. We may think of engulfment in terms of the mother of the allergic child (of course, this is not only true for mothers of allergic children) who often has preconceived notions of what her little girl should be like. If the mother is immature and in-

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capable of dealing with the physical and mental growth of her offspring in a mature way she inevitably must fall back upon patterns which arise from her own immaturity. These patterns, so often obvious in narcissistic women who have never been prepared for the mature responsibilities of womanhood, represent an attempt to coerce the developing child into a pattern consistent with parental ideas of what the little girl (and in the case of the father, what the little boy) should be. The developing child, handicapped by a rigid, narcissistic mother and by eczema or asthma, is forced during development into a distorted state of dependency. Not only is the child incapable of meeting the demands of the parent to conform to the parent's immature ideal, but the child also has its developing independence and maturity constantly threatened by the engulfing parent. Then it is that the frustrated mother becomes enraged and threatens the child. There is the additional frustration which the parent faces in the child's illness. When possible, every act of the child is observed by and manipulated by the parent. This cannot be termed rejection, nor can it be fairly considered a compensation device for a strict, unconscious rejection, for these oversolicitous parents often openly show their rage, and beat their children. The raw rejection theory gives no understanding of the mechanism but only a fraction of the end-result. It is the mechanism of engulfment by the parent which stifles independence, maturity and the physical and mental health of the child.

We shall see that the notion of rejection does not provide the physician with sufficient therapeutic material for the rapid development of insight in parents and in patients. The notion of engulfment is more successful in explaining to patients and parents the nature of the difficulty and practical ways of solving some of them. We might say that the parent is inextricably bound to his child in the same way that Adam felt when Eve was created. May I quote Genesis, Chapter 2, Verse 23?

"And Adam said, This is now bone of my bones, and flesh of my flesh: she shall be called Woman, because she was taken out of man."

COMPARISON OF MATERNAL OVERPROTECTION AND ENGULFMENT

The proposed concept of incorporation or engulfment can be connected only to a limited extent with the portrayal of the overprotective mother by Levy.[2] Levy states the idealized case:

"When overprotection is revealed by all four criteria, the picture presented is well portrayed by a mother who holds her child tightly with one hand and makes the gesture of pushing away the rest of the world with the other. Her energies are directed to preserving her infant as infant for all time, preserving it from all harm and from contact with the rest of humanity. For her child she will fight hard, make every sacrifice, and aggressively prevent interference with her social monopoly. Her aggression, directed so strongly against the intruder, yields, however, before the child. Towards him she is submissive; her discipline falters when he becomes assertive in the latter half of infancy, and is gradually destroyed."

Levy's formulation may be contrasted with the present formulation of engulfment in an idealized situation for both the father in relationship to the son and the mother in relationship to her daughter. The formulation is based upon the analyses from which the verbatim data in this report are taken, as well as the notions of Sperling and Lidz and Lidz. In the present formulation, following for comparison the preceding paragraph, the parent holds the child tightly with one hand and pushes the rest of the world with the other when the rest of the world does not fit in with the fore-ordained concepts of what the engulfing parent wishes to do with its allergic infant. Energies are thus directed to preserving the infant as an infant but only in so far as the narcissistic drives of the parent determine the gain to be held by preservation of infancy. These parents sacrifice everything both on a symbolic and realistic level to have their child develop in the way to satisfy their own narcissistic social compulsions which are often well organized and consistent with socially acceptable and desirable goals. Aggressions are not necessarily directed against the intruder and do not necessarily yield before the child except in those instances where the desires of the child and of the aggressor stimulate the anxieties produced by the parents' immaturities. Toward the child the parent is neither submissive nor dominating but is always a complicated mixture of both, depending upon the neurotic gains to be made in return for either aggression or submission.

I am inclined to agree with Levy (page 116)[2] that studies of maternal attitudes by the method of psychoanalysis indicate that hostile feelings toward children are universal in our culture. It is not unexpected, therefore, that the high number of rejecting mothers in Miller and Baruch's series[4] is as high as it is but it is unexpected that it was as low as found in their control series.

Undoubtedly, unconscious rejection resulting in oversolicitousness does occur as in the following instance, but this is often a symptom and in my studies does not represent the basic psychodynamic force.

Case 1.—A girl of three with eczema was brought by both parents. A box of candy was on my desk. The child saw the candy and I offered her a piece of candy, which she took. The father, in a horror-stricken voice, asked, "Did that piece of candy have a nut in it?" As I told him that it contained a nut he dashed over to the child, put his fingers in the child's mouth, removed as much candy as he could from the mouth, carried her off in his arms to the bathroom where he washed out the mouth, and returning announced, "She's allergic to nuts." It may be added that later studies disclosed that the eczema began when the child was sixteen months old and when the nurse had been suddenly discharged.

In the following case, a four-year-old girl with eczema of the buttocks for one year following a barium enema, is shown open rejection by the mother born out of hostility. This does not appear to be the cause of the child's eczema as the eczema cleared in spite of the rejection when the actual factor was apparently discovered and worked out.

Case 2.—A barium enema was given to the child (at age of three) as a diagnostic procedure because of obstinate constipation which had lasted almost two years. The baby's first symptom (at sixteen months of age) was crossing her legs and she acted as if she were afraid to have a bowel movement. After several interviews with the child and with her mother it seemed likely that the child, who slept in the same room with a brother six years older than she, might have experienced an accidental seduction at sixteen months of age. The mother was advised to give the child her own bedroom and her relationship with her children was the subject of several therapeutic interviews. The mother came in for the fifth interview appearing rather disturbed and said, "Her rash is 90 per cent better than when I first came here. Why should it happen? You haven't done anything! My child's eczema is her problem. Why can't she go to a psychiatrist when she grows up?" She stopped coming after the sixth interview. Immediately following this, the eczema cleared up completely for one year.

A common type of engulfing parent who demands that the child live up to his own standards is illustrated by the following case.

Case 3.—A vigorous, aggressive, energetic man brought in his eleven-year-old son with a deformed chest who had been in status asthmaticus for some time. The tenor of his conversation was that he could not understand how he could have a son who was not on a par with his own physique and talents. When I mentioned that I felt all restrictions which had previously been placed on the boy should be removed so far as possible he at once said that I was the kind of a doctor he had been looking for and he felt that his son could do everything, and he co-operated in every way helping his son to recover from his serious asthma. Insufficient material is available in this particular case to give a suitable psychodynamic formulation but this type of parent is not rejecting except where the child's illness is concerned. This parent rejected his sick son but accepted his well son. It is much simpler to deal with this type of parent because psychologically he is ready to co-operate with the physician in getting the son well so the son can fit into the pattern demanded by the parent.

The rejecting parent shows guilt when the child is in danger symbolically. The engulfing parent demands narcissistic satisfaction regardless of any danger to the child.

"THAT'S MY BOY"

Allergies to food and the resulting syndrome of eczema, asthma, hives, migraine, et cetera, often have their origins in early childhood. The attitude of the mother toward foods as well as the position taken by the pediatrician such as, "He'll outgrow the food allergy" or, "Nothing can be done," sets up memory traces which influence future life as an adult and his response to future medical care. The child may outgrow his allergy to food but not his frustrated desire for parental affection if the foods were not the real cause of the symptoms, as is often the case. Therapy includes both an understanding of the significance of the laboratory findings such as the different significance of positive and negative allergy tests, but also, for example, the intricate psychologic consequences of finding either positive tests or negative tests. The doctor is expected to deal with all the origins of allergic symptoms. In the instance of the

child, it is usually a primary interest of the parents to avoid criticism of their own relationship with the child, and to prevent the doctor from exploring threatening parental patterns. In this connection I shall shortly give an example of parental engulfment of a boy by his father. Parents are often unconsciously grateful to the doctor who avoids pointing out an unsuitable child-parent relationship and who deals directly with the allergic symptoms on a strictly physical basis. The quasi-hypnotic effect of a doctor stating the symptoms are simply due to foods may be illustrated by an experiment which I performed some years ago. A forty-year-old woman, who had been in a concentration camp in Germany for five years and who had pointedly complained that the bread was not good at the concentration camp, had giant hives. These hives had persisted for many months and had not responded to pharmacologic therapy. During her allergy skin tests which were definitely negative, I arranged to put a 1:1000 histamine solution in a bottle labeled "wheat" but only containing histamine. She saw the bottle and the label. The violent skin reaction, which from the unmistakable point of view of the laboratory and to her way of thinking, meant that wheat was the offender. A wheat-free diet was prescribed and her improvement was dramatic. Her hives practically disappeared and her mood improved. Needless to say, after several months on the wheat-free diet her giant hives reappeared in spite of the absence of wheat in her diet. Similarly, psychologic effects of placing a child or an adult on a diet for symptoms made responsible by an authoritative figure are thus brought out experimentally.

The longer a memory trace has been planted the more this memory is invulnerable to change. The incorrect interpretation of the skin test by the child, the parents of the child, and the doctor often determines what the future emotional life of the patient will be. It is common practice in therapy to psychologically affect the allergic patient by crystallizing false memory traces through diet just as I produced a fictitious allergy to wheat.

In Case 4 are extracts of verbatim recordings of psychotherapy of a single young man of twenty-five who had had eczema for several years complicated by rather severe asthma. After fifty hours of psychotherapy in which little progress was made the patient saw a motion picture entitled "That's My Boy." After seeing this motion picture in which the father attempts to have his son follow in his own, and, needless to say, narcissistic footsteps, without any regard for the personality and physical make-up of the son, the patient came in and said, "I know what you have been trying to tell me, doctor. I saw a movie last night and the father wanted the son to be just like him and the boy couldn't be. That is my trouble."

The minor role of the diet in the patient's syndrome of eczema was dramatically demonstrated to him when a conflict situation involving authority was created at work under conditions where diet could not be considered an adequate explanation for the itching and scratching. This

was possible only after the patient had insight catalyzed by seeing the motion picture during therapy.

Case 4.—X was a twenty-five-year-old single man who had had a very severe, often completely incapacitating, eczematous dermatitis fluctuating in severity for about ten years. Asthma began at the age of ten. His referring physician wrote, "Rowe's fruit-free, cereal-free diet was prescribed." Scratch tests by another referring physician disclosed positive reactions, to yeast, pyrethrum, cat dander, and feathers. Intradermal tests showed sensitivity to ragweed, sheep dander, orris, dust, flaxseed, horse dander, goat dander, rabbit dander, glue, tobacco, horse serum, wheat, chocolate, green peas, milk almond, herring, silk, kapok, mixed trees, cow dander, celery, cherry, orange, sweet potato, cauliflower, salmon, mackerel, cucumber, beets, asparagus, pear, grape, grapefruit, prunes, raspberry, clams, pineapple, oyster, shrimp, pepper, molds, Monilia, Penicillium, and Trichophyton.

It appeared during the course of psychotherapy that X was able to eat everything under two life situations, which clearly indicated that diet alone could not account for the clinical course. For example, when he was on active duty with the armed forces undertaking dangerous missions his skin cleared up completely only to break out again shortly after returning home. Early in the course of this illness while away from home, for a period of months, and while he was enduring certain hardships, his skin again cleared up irrespective of his diet. The fact that his itching and scratching could occur independent of allergic reactions and explicitly related to a threatening situation embodying his underlying conflict was brought out in an incident which occurred after fifty visits. At work, he was faced with the possibility of being subjected to the anger of two different father figures, both of whom informally supervised his work.

Patient: "Now, another thing today was bothering me at work. I mean so far everyday at work, I just seemed to forget about the skin and I felt fine. But today the boss's son—there are three grinders in the shop, one was disconnected, and one is not automatic and the other automatic one was used, and I had to use the automatic, so I had nothing else I can do, except to use the machine, so it's being used—so I went over to the boss's son and I told him. So he said, 'All right, I'll start you on another job.' So he gave me a blueprint of a part and I had to make a fixture to hold that part so that holes could be drilled in it. And he said, 'Now it may look easy to you, but the blueprint is only the picture of the part; now you're going to have to figure out by yourself, how the fixture is going to work, to hold it, and it's going to be mass-produced so the piece has to be able to be taken out from the fixture easily and put in again easily.' So, he gave me the print, and I went to my bench and I started figuring out a way it could be done. I had another job that was not the same thing; it was close to the same thing. So I took a look at that fixture, how it was made and from it I got a couple of ideas. So, then I had been working my drawer and it took me about two minutes something—like; so the boss's son came over and asked me how I was making out so I told him what I had done and what he thought about it. So he said it was all right and he gave me a couple of ideas of how he would make it. So—some of it contradicted my ideas, not so much that his wouldn't work, not so much that mine wouldn't work, but in his respect he would have done it that way; but in my respect I would rather have done it the other way. But just because he mentioned it, I didn't like his way of doing it, as much as I like my own, or just because he mentioned it, I felt that I had better do certain things that he had mentioned. Then this old German fellow that works there, he came over and he said, 'What's the matter you're not working on that other die anymore?' So I told him, no, I have to get into the grinder and meanwhile, Arnold gave me this to do. So he took a look at the print and he saw what I had drawn up myself, plus the ideas from the boss. Now, he contradicted my ideas, as well as the boss's ideas, so not wanting to—now he is very friendly with—I mean, the boss's son he contradicted—now he is friendly with the boss, they both come from the same section in Europe—but they're very friendly, so now I didn't know what to do and at that point, there was no figuring out how to do the job, how to make the fixture. Now it was a way to please Jack and to please this German fellow, and that's when my itching started. And it's been bothering me—well, I got that job about 3 o'clock and it's been bothering me ever since."

Doctor: "What do you think started the itching?"

Patient: "Well, all I can see is from when it started is that it wasn't after I just ate something. It was—and it wasn't when Jack the boss's son gave me the job or when he came over to give me the ideas. It was when the other man came over to give me his idea, and they counteracted the orders of the son's and my fixtures."

Doctor: "Well, talk about that—and your feelings about it—that's precisely what we're driving at. Now, what were your feelings when your itching started?"

Patient: "It wasn't the feeling so much as to what I felt at the time. It wasn't the feeling of what I—the itching actually started when I tried to figure out a way that it would be incorporating, Jack the boss's son's idea and the other man's ideas—to try and incorporate them both so they both would see that I wasn't—in other words, my ideas were all forgotten now, because they were both correct and mine were correct too. But if I used mine I haven't got the experience that the boss's son has, and also that this other man has. So, if something goes wrong and I do it my way, then I'm in trouble, but if something goes wrong and I do it their way, then I'm saved a little bit of trouble, I mean it's all according to how the trouble goes about due to the way it's made, due to the design of the fixture, then I'm out of the trouble because it was given to me by them, but then it was just the itching when I tried to figure out a way to incorporate all the ideas to show that I wasn't—that they're talking through their hat, and after they got finished telling me, then I turned around and do it in a different way."

Doctor: "That's very important. As you put it the itching started when you tried to incorporate both their ideas. Now another thing that's important here, you just told me that all three of you had ideas which were correct. So this wasn't a technical problem at all; this was a problem in which you tried to please two different people at the same time, each of whom was a person in authority, the boss's son, because he was the boss's son, in fact you even called him the boss accidentally. And the old German is in authority, because after all he knows a great deal, he is an authority in the field, you respect his judgment. You wanted to please both, you were afraid of the criticism of either, isn't that so?"

Patient: "Well, not so much the criticism—"

Doctor: "Or the displeasure."

Patient: "That's it, that's more or less it, that they don't think that I show I'm a know-it-all, or something like that. In other words, let me put it this way—there'll be a time in the future when I don't know what the next step will be, and I would have to ask them; and then they'll say, 'I showed you something previous to that and you went ahead and did it another way, so now go ahead and figure it out for yourself.'"

Doctor: "But you started to scratch when you considered that you were in a jam with, so-to-speak, people who are over you, isn't that so?"

Patient: "Yes."

Doctor: "So, that's one of the things that makes you scratch, when your superiors place you in a position, where anything you do will lead to displeasure or disapproval."

Patient: "Yes."

Doctor: "There was no way of your pleasing both?"

Patient: "Even in the most basic fundamentals, the boss's son told me to use three-fourths inch material and the old man told me to use one-half inch material, even from the basic start of the jig it was wrong."

Doctor: "Now, practically speaking, let's talk about what you should do in the matter. How can you get out of this jam?"

Patient: "Well, first of all I intend to start off with five-eighths material."

Doctor: "I see, you're going to play it safe."

Patient: "Yes, but after that I don't know. If everything comes out right the way I do it, neither of them would have any complaints, because if it works there wouldn't be no complaints from the old man or the boss's son, but if I get stuck later on that something wouldn't work properly, then I'll be getting it from two sides. And if I do it the way the boss's son said, and something goes wrong, I'll be still getting it from two sides; I'll get it from the old man and I'll be getting it from myself saying, Why didn't I do it my way?"

Doctor: "Would it be possible to sit down with the boss's son and tell him of the difficulty you're in, that you like to get advice, that you're trying to learn and that you find that you would get either less displeasure or that of the old German . . ."

Patient: "Well, the boss's son told me, after he left, he said, 'That's a couple of ideas I have, but you do it whichever you feel is best.' Even with him saying that, it still doesn't mean anything, it means that if I don't incorporate his ideas, he is going to say, 'Now—I gave you a couple of ideas.' . . ."

Doctor: "Are you sure you don't think of him as you think of your father? Are you sure that you aren't visualizing them both deep down, as people who would

criticize you the way your father would criticize you? These are two different people who are not unlike your father. And that's why your scratching started, because you, so-to-speak, are wedged in between two fathers, symbolically or emotionally speaking?"

Patient: "It's possible, I mean—"

Doctor: "What do you think of that? Go ahead and talk about it. Certainly the father is the boss; your father is an old German, too."

Patient: "Yes."

Doctor: "So, here you're lined up between two fathers, really."

Patient: "Well, as far as I could see it—I could do it my way and nothing would go wrong. I could do it the old man's way and I could do it the way the boss's son wanted and nothing would be wrong; but there is always the possibility and no matter whose way I chose, somebody may or may not be hurt by it; I don't know. And to try and do it both ways is impossible, because some of the ideas are so far apart that they can't be incorporated. Of course, in some parts I could use one idea and in some parts other ideas, but that would get confusing. I mean, as far as I'm concerned I would rather do it my way, and I have to take my chances that everything would work out all right. Maybe you could tell me what to do, or not tell me, offer no advice, but it's just the idea, it's as you said, it's like my father; that I will have to go back to them some time in the future for advice and if I don't accept it now, when I need it I may not get it."

Doctor: "Well, I'm not sure you're right there, that you have to decide for yourself, but remember these people are not your father. One is the boss's son and the other is another worker there like you. And if you leave the job, there's still another job but you don't leave your father; the loss of their friendship isn't the same as the loss of your father's love. It's very different, so you mustn't treat these people as if they were your father."

The verbatim recording illustrating Case 4 shows the results of a typical case of engulfment where the basic love of the father for his son as far as I could determine was unquestioned, but it was unfortunately overshadowed by his own narcissistic desire to have a son created in his own image.

After approximately 150 psychotherapeutic interviews in which the patient was able to gain insight into his relationship with his father and father surrogates he gradually was able to utilize that insight to achieve sufficient independence to marry and leave home. He went West and is now residing in another state. In this case I believe that psychotherapy should have continued for a longer period although the follow-up may show that the patient's insistence on breaking off with all father figures including the doctor may have been best.

"MOTHER STORY"

Case 5.—This was an adult woman of thirty who had persistent and severe eczema, asthma and hay fever. The eczema had begun in infancy. The patient, Alice, had many years of somatic therapy with an increase rather than a decrease in her symptoms. During psychotherapy it became apparent that the patient's relationship with her mother was not that of simple maternal rejection but closely approximated engulfment by a domineering, narcissistic woman who was generally endeavoring to solve many of her own emotional conflicts by stifling the independence of her child as she had that of her husband and of all those vulnerable who came in contact with her. While I grant that the threatening nature of the mother's attitudes can be superficially labeled rejection, the intrinsic psychodynamic formulation is better understood by viewing the mother and daughter as an interdependent unit in which mother and child retain the fusion of the relationship between the mother and the nursing infant, so to speak, well on into adult life. The child, although frightened by the mother, is even more frightened at the threat of the loss of the

domineering, semi-hypnotic, psychological force which the mother unremittingly exerts on the child. The intensity of the relationship even into adult life can perhaps be best expressed by the verbatim report screened to include only what she said about her mother in the first fifteen interviews with this patient. These have previously been published.[1,b] The analysis of this patient was mainly concerned with removing her psychologically from the engulfing mother, and developing within her a sufficient number of her own assets of independence by which the mother herself had been threatened and therefore were repressed by the child.

Remarkably enough during psychotherapy the patient regressed to the age of two when she recalled a beating by the mother for playing with a doll. Psychotherapy based upon the type of psychodynamic formulation hitherto given has resulted in the following clinical improvement. The patient, following psychotherapy, had no eczema, asthma, or hay fever during the pollen seasons of 1947 and 1948 as well as during the entire year except for extremely minor episodes of scratching during emotional tensions created probably by the stresses of the psychotherapy itself. Perhaps it might be best to allow the patient to tell in her own words of the results of therapy based on the foregoing formulation of engulfment (or introjection) rather than rejection. This patient was presented as part of a progress report as the meeting of The American College of Allergists in 1953 in Chicago.

Patient: "The first and most important thing I think that I'll never be able to forget, and it will always mean something to me, no matter if I, even if I stay at the point that I'm at now, and that is I remember the physical condition that I was in when I first started. I don't think I could have been much sicker, physically, so covered with a rash from head to toe, and to find that I'm at a point now where my skin is never in any condition where I'm afraid to go out as I used to be or ashamed to go out. I don't feel that I, that I have to stay close to home, to hide myself. I find, too, that even though I have moments of depression even now, which is great, is certainly not as consistent as what it used to be even though I am depressed. Very often, I, I can realize now that it's only because I'm more or less in the middle of a fight, of a battle, to get through and understand why and what instead of just commiserating with myself and feeling sorry for myself, and then taking it out by scratching. More, I feel also, that the analysis has given me more of a feeling of security. What I used to, well, I, I remember myself thinking almost continuously of either not being clever enough, of being suspicious of other people trying to make a fool of me, of recalling embarrassing situations consistently, and all these with the rather distressing—this of course, I, I took a long time to realize and to get over because I had such a feeling of dependence upon my mother and not upon my mother at the time when it would shift to my husband. Then, too, although I've lost my, lost my mother in the meantime, I'm still able to recall that I was able to see through the situation that I had with my mother, and although I had identified myself completely and probably still do at times, the identification is not as complete or as tight as it used to be. And then another state of thing that I remember and very much aware of is that the way I handle or rather handled my child. If I had continued in the way that I was doing I feel what would have happened to her—it would have been the most sad child of the result. I feel now that she has more opportunity for developing into a much more wholesome person because I myself am more wholesome. My relationship with my husband certainly could not have been any worse—I don't think other than to divorce him at the time."

Doctor: "Before you go into your relationship with your husband I'd like at the beginning of your discussion to clarify your physical status. As I recall it was about one and a half years ago, or a little more, that you, or after about two years of treatment, that your skin really cleared up. Is that correct?"

Patient: "Yes, that's correct."

Doctor: "Now, you went away to camp that summer and that was the summer of 1947. It's now 1949 and in the summer of 1947 you were in the same pollen area to which you had gone for many years. Now, did you have any eczema that summer?"

Patient: "I had no eczema that summer."

Doctor: "Did you have any asthma?"

Patient: "I had no asthma."

Doctor: "Did you have any hay fever?"

Patient: "And I had no hay fever."

Doctor: "Now, when you came back to New York, you had, as I recall, a certain amount of eczema, which cleared up, after certain problems were solved. Is that right?"

Patient: "That's right."

Doctor: "Now, then, during that year, of what would be the percentage of skin improvement, that you had, would you say?"

Patient: "Well, I would say 99 per cent."

Doctor: "And then you went to summer, to camp again, in the summer of 19—."

Patient: "'49, '48."

Doctor: "'48, yes. And did you have any eczema, asthma or hay fever?"

Patient: "I had nothing again, that summer, at all. And, in fact, I would say that my problems that summer were even greater than what I had experienced before, in that I had to live with two people who were in constant conflict with each other and I was the one who had to control the situation. It was the first time that actually, anything of this sort had happened to me where I was the more or less, the leader and the guide and I was able to come through this, although there were many distressing moments, and many times when I felt under extreme tension between the two people. I still did not resort to, to scratching, or to, nor did I have any asthma nor anything else."

Doctor: "In other words, then, you were able to deal with these situations in terms of difficulties of the situations themselves and not the effect of that. Your allergic symptoms were not affected by the emotional tensions in which you found yourself."

Patient: "That's right."

Doctor: "Now, then, your mother died in October, 1948. I think you began to scratch just a little bit at that time. Is that right?"

Patient: "Yes, I did."

Doctor: "It was just about one corner of the face. Is that right?"

Patient: "Yes, it was just in the corner of my eye, it's slightly—."

Doctor: "And then have you had any since?"

Patient: "No, I haven't had any since.

Doctor: "And have you had any asthma since?"

Patient: "No, I have had no asthma."

Doctor: "But you did have some sneezing attacks haven't you?"

Patient: "Yes."

Doctor: "So that's your only allergic symptom that you've had now, in about, in almost two years."

Patient: "That is the real, only real allergic attack that I've had is the sneezing, and that has only occurred twice. I think, too, that I'm able to, to live with another person who has faults, as we all do. And although there are many things that I still can't accept, there are still some things that I do. There's another important item that, about analysis, which, perhaps I, I didn't talk too much about during my sessions, but which I think have a great deal of meaning to me. And that is, I placed all values of life upon material things. To me, happiness could only be gained by having a good deal of money, or a good deal of clothing, or other luxuries. I realize now that I could have all the money in the world and to be in the state that I was in, when I first started analysis it would do me no good. It wouldn't give me my health nor the outlook upon life that I have now. I think, too, that the one thing that, that I've gotten from analysis so far, which, of course, means that greatest to me—all these things, I, I can think about and I can accept, but, of course, the physical part of it is the most important to me. The fact that I don't have these severe asthma attacks, that my skin is in a healthy condition, and that I'm not afraid to go out and meet people, that, when I have an invitation, I don't have to stop and think about what I'm going to wear, or how I'm looking, and worry about it . . . I also, too, can appreciate the fact that, for a couple of years, even after I was going to analysis, I had a child who jumped every time I raised my hand, whether it was towards her, or not. And now, she is a child who, who can say, who can talk about other children and their mothers who spank them, and she doesn't get spanked. A child who was terrified of her mother and now talks to her, fools around with her, and feels comfortable with her, and in fact, desires my company. . . . Well, there are many, all these things, that, that I see, accomplished have made me into more of a person. I am not yet, been able to put myself into a setting more or less, of deciding just exactly what I want to be, or where I want to go with myself, so to speak. What do I want to accomplish now? I've accomplished this much now. What am I going to do with myself? Before, I couldn't do anything except scratch. I was lost. I'm at a point now where I want to go somewhere. I don't want to just sit home and, and keep on scratching. I want to go out and, but when I say, go out, I mean I'm willing to stay home and

be the housewife, if it, that's the best thing for me to be. But to be a, but to accomplish some sort of position in life, in a business-wise way! When I fight for something I want it to be what I know what I want, not that I'm groping any more. I want to fight for something that I really know that it's for me."

DISCUSSION

The foregoing method of presenting psychiatric data by the use of verbatim transcripts removes the results of psychotherapy from the anecdotal technique to a more scientific frame of reference. I believe that much of the confusion and disagreement in the field of psychosomatic medicine today could be reduced if more scientific data were made available to the allergist. The argument that the allergist is not equipped to deal with concepts of this type, I believe, is based primarily upon the difficulty of communication between those who are formulating psychodynamics and those who are not. There is no fundamental reason why these barriers of communications cannot be lessened, or eventually in the coming years, be eliminated entirely. The concept of maternal rejection, for example, is difficult to use in brief psychotherapy with the parents of allergic children. Indeed, it is difficult for both the physician and the parents to accept this concept not only because it is incomplete but because it does not adequately represent the complicated emotional conflicts that these parents undergo. The notion of engulfment and domination can be readily utilized by the allergist. I have found that it is more acceptable to the parents of allergic children.* These parents often can readily see that they desire to have their children develop in their own images of what their children should be. This fits in with what they know consciously and often readily admit. Clinically speaking, this is also readily understood by parents. If acceptance of the engulfment theory and the use of it effectively by parent, allergic patient and doctor is not followed by improvement another mode of therapy should be tried. I believe that most often after the parents understand the importance to them of having their child adapt to their own narcissistic needs, the threatening nature of the rage engendered by the frustrations undergone by the parents decreases and the derived rejection of the child automatically becomes much less. This is the goal of therapy.

SUMMARY AND CONCLUSIONS

Although the treatment of the allergic patient should begin with the study of his allergic hypersensitiveness from the point of view of specific antigens, it should not end at that point. This beginning, especially in cases where the therapeutic results are unsatisfactory, should be supple-

*We may think of the syndrome or complex in terms of Cronus who, in Greek mythology, was the youngest of the Titans. His mother Ge, the earth, imprisoned him in her body. After Cronus' mother Ge castrated Uranus with a sickle and tossed the severed member into the sea, Cronus became ruler of the universe. Cronus was warned that one of his own children would supplant him and as his sons were born he swallowed them. Zeus was saved when Cronus was given a stone when Zeus was born. Should we call the syndrome of the engulfing parent a "Cronus complex"?

mented by instruction of the patient in matters other than antigenic sensitivity. He should be instructed to look for personal sensitiveness, that is, to emotional tensions within himself in response to people—not only to things; to attitudes—not only to chemicals; to feelings—not only to unknown or ill-defined allergens. These sources of emotional conflicts within him may be sought in the home, at work, and in his goals focused in the community at large. The physician who by nature and interest is willing to deal with certain of elementary aspects of psychotherapy should bear in mind that the allergic individual may either have had a childhood in which parental domination and engulfment prevented his growth of independence or where in adult life this dependency upon a demanding, engulfing parent has not been replaced by mature relationships. Parental rejection may occur when the parent becomes enraged at the failure to form the character of the allergic child in a pattern based upon the parent's own narcissistic needs. The physician who includes this methodology in his therapeutic program of the allergic patient will probably find himself richly rewarded not only by better therapeutic results but by himself gaining more insight and more appreciation of the dramatic emotional episodes occurring within the inner life of the patient and the relationship of these episodes within the patient to his allergic symptomatology.

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133 E. 58th Street

TREATMENT OF RHEUMATIC DISEASE BY DESENSITIZATION WITH AN AQUEOUS EXTRACT OF STREPTOCOCCI

I. Fibrositis and Hypertrophic Arthritis

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FIBROSITIS is the most common rheumatic disease. Scarcely anyone goes through life without experiencing one or another of its various manifestations. Pathologically, fibrositis is a simple inflammatory reaction in white fibrous tissue. Common localizations appear in the muscles, bursae, tendons, and capsules of the joints. Clinically, stiff or wry neck, lumbago, subdeltoid bursitis, tendonitis and "capsular arthritis" are the most frequently encountered primary fibrositic conditions. Secondary fibrositis is a feature of many diseases. It is a minor manifestation of rheumatoid arthritis, but in hypertrophic arthritis it assumes greater significance because it accounts for much of the patient's discomfort.

Pain, stiffness and tenderness are outstanding symptoms of fibrositis. The so-called resting stiffness which "freezes" the patient in the position assumed upon resting after exercise is a constant symptom, and its observance is most useful in following clinical progress. This stiffness is relieved by complete rest, but when severe it may persist throughout many hours of rest. It frequently is troublesome upon waking in the early morning. Less severe involvements may have much resting stiffness during the first few hours of rest, but it disappears with overnight rest. The length of the period of rest required to overcome this stiffness may provide a clinical indication of the severity of the fibrositis.

The pain in acute fibrositis may be so severe as to preclude all movements. In the subacute stage the pain is of a persistent, aching character. It may shift from place to place without obvious cause, and may radiate along nerve trunks. Regional pain is the rule in involvements of tendons, bursae, and joint capsules. First movements may aggravate the pain, but in mild cases later movements tend to reduce the stiffness and to ease the pain on motion.

Tenderness is present over the affected bursae, tendons, and nerve trunks. Tonic spasm and tenderness may appear over the involved muscles in the more severe cases, but in the milder ones tenderness may be present only over their attachments to the bony prominences about the joints. Firm pressure over the inner condyles at the knee, or over the epitrochlears at the elbow constitutes a convenient test for this type of tenderness in fibrositis.

Objective symptoms may not be prominent but are regularly present in fibrositis. Limitation of motion, tonic spasm in muscles, distension of bursae and tendon sheaths are usually demonstrated without difficulty. Fibrositic nodules appear less commonly but are distinctive. They may be

noted on the superficial tendons of the hand, about the capsules of the more superficial joints and within the muscles.

As early as 1927, our studies revealed an extreme sensitiveness of the tissues of patients with rheumatic fever to the products of streptococci.[4] Swift in 1928[7] suggested the term hyperergy, for this unusual phenomenon. This hypersensitiveness appears to be a feature of the rheumatic state, being exhibited also by patients with fibrositis, rheumatoid arthritis, and hypertrophic arthritis, as well as by those with other forms of rheumatic disease.

In spite of the rather widespread discussion at that time of this hypersensitiveness to streptococci as an etiological factor in rheumatic disease, few attempts were made to develop a method of treatment based on it. More recently, especially since the publication of the reportedly favorable responses of these diseases to cortisone and corticotropin (ACTH) have been noted, attention is beginning to be directed to this possibility.[1,2,3,6]

In this paper we are reporting on our experience with the treatment of fibrositis and hypertrophic arthritis by desensitization. In our first studies of rheumatic disease, we used a suspension of streptococci which we injected subcutaneously. The suspension was soon supplanted by an aqueous extract of streptococci* (AES). The minute doses of the extract which we used in the present study were arrived at gradually. The method was reported in 1940.[5]

CLINICAL MATERIAL

For purposes of simplicity of presentation, a small cross section of our experience is recorded in clinical data of eighteen patients with fibrositis coming consecutively to the office for the first time during the three months from March 5 to June 5, 1951. An additional patient (A14) was selected to show the relationship of allergy to dust and fibrositic symptoms. Five of these were diagnosed primary fibrositis, and fourteen hypertrophic arthritis with its attendant secondary fibrositis. A clinical tabulation of these patients is presented in Table I. Brief abstracts of the histories of three of them (F1, A5, and A14) are recorded in order that they may be correlated with progress developments as shown in Charts I and II.

It is significant that of the five patients with primary fibrositis, three had acutely hyperemic throats; one, several infected teeth; and one, infected tonsils. Of the fourteen patients with hypertrophic arthritis, one had a history of sciatica; and two a history of acute bursitis. It was observed that one had diabetes; two, cataracts; three, infected teeth; five, large suspicious tonsils; and five, arterial hypertension.

*A non-hemolytic streptococcus (S. cardioarthritidis, a strain of S. salivarius—Bergey's Manual) was grown in nutrient broth and washed free of the liquid medium. The extract was prepared by suspending the streptococci in normal saline in a concentration of 100,000,000 per cubic centimeter. After an extraction period of seven days in the refrigerator, the bacteria were removed by filtration. For clinical use, a series of dilutions were made in neutral buffered saline and preserved with 0.5 per cent phenol.

TABLE I. FIBROSITIS AND HYPERTROPHIC ARTHRITIS
NINETEEN PATIENTS

Subject	Date 1951	Age	Sex	Diagnosis	Duration	Chief Complaints and Symptoms
F1	3- 5	44	M	Fibrositis	3 mos.	Tenderness, stiffness and pain in both elbows.
A1	3-20	54	F	Hypertrophic Arthritis	8 mos.	Pain in lower back and down the right leg. Stiff, deformed fingers.
A2	3-22	51	F	Hypertrophic Arthritis	1 yr.	Tenderness, stiffness, and pain in fingers. Stiffness in left shoulder and knee.
A3	3-28	64	F	Hypertrophic Arthritis Diabetes	10 yrs.	Stiff, enlarged, tender digital joints. Painful lower back.
L.R.*	4- 4	25	M	Fibrositis	6 yrs.	Pain in arms and legs. Stiffness in hands and knees.
F2	4-13	32	F	Fibrositis	6 yrs.	Pain and stiffness in neck, and shoulders and arms.
A4	4-23	68	F	Hypertrophic Arthritis	6 mos.	Pain in neck, shoulders, ankles, and lower back. Enlarged and tender digital joints.
A5	4-23	62	F	Hypertrophic Arthritis	1 yr.	Pain, stiffness, and deformity of hands and knees. Tenderness over right sacroiliac.
F3	4-24	32	F	Fibrositis	3 yrs.	Pain, stiffness, and muscle spasm in lumbar region. Pain and stiffness in knees and left wrist.
A6	4-25	58	F	Hypertrophic Arthritis	10 yrs.	Pain, tenderness, stiffness, and deformity of fingers. Subacute bursitis right elbow.
A7	4-30	58	F	Hypertrophic Arthritis	12 yrs.	Pain, stiffness, and deformity of fingers. Pain and stiffness in neck and lumbar region.
A8	5- 1	79	F	Hypertrophic Arthritis	35 yrs.	Pain, tenderness, stiffness, and deformity of hands. Pain and stiffness in knees, and ankles.
F4	5- 7	36	F	Fibrositis Sciatica	1 yr. 6 days	Pain and stiffness in hands. Acute pain along left sciatic to foot for past 6 days.
A9	5-15	59	M	Hypertrophic Arthritis	2 yrs.	Pain, stiffness, limitation of motion in knees, and lumbar spine. Stiff deformed hands.
A10	5-18	49	F	Hypertrophic Arthritis	6 yrs.	Stiffness and pain in lumbar spine. Stiffness, deformed fingers.
All	5-28	61	F	Hypertrophic Arthritis	8 yrs.	Pain, stiffness, and deformity of knees and hands.
A12	5-29	42	F	Hypertrophic Arthritis	12 yrs.	Pain, tenderness, stiffness, and deformity of hands. Pain and swelling of knees.
A13	6- 5	54	F	Hypertrophic Arthritis	4 yrs.	Pain, swelling, tenderness, and limited motion in knees.
A14**	1- 4	70	F	Hypertrophic Arthritis Multiple allergies	20 yrs.	Pain, swelling, tenderness, and deformity of hands and knees. Allergic Bronchitis.

*Inadvertently missed in preparing Chart I. Relief prompt and complete. Last of six treatments 5-17-51.

**Selected to show relation of allergy to dust, eosinophilia, and fibrositic symptoms.

METHODS

A detailed clinical history of each patient was taken. A general examination, and laboratory studies including routine urine examination, blood counts, blood sugar, blood urea nitrogen, blood uric acid, Kahn test, sedimentation rate of erythrocytes, and direct eosinophile counts were made. Roentgen ray studies, metabolism tests, or other special studies were made as appeared indicated. At the time of the first visit each patient was given subcutaneously an injection of the aqueous extract of streptococci (AES).

The patients returned for second observation from twenty-four hours to seven days after the injection, and at intervals of from one to three weeks at subsequent visits. Sedimentation of the erythrocytes and direct eosinophile counts were made at these times. The intervals of treatments, the dosage of the aqueous extract of streptococci, our estimate of clinical symptoms, the results of sedimentation tests and of eosinophile counts are recorded in Charts I and II. In chronic cases each serves as its own best control throughout the prolonged period during which the symptoms were not controlled by previous treatment. These periods are indicated at the beginning of the symptom curve in each case. In addition, the record of patient A14, shows failure to respond to too large a dose, relapse when an

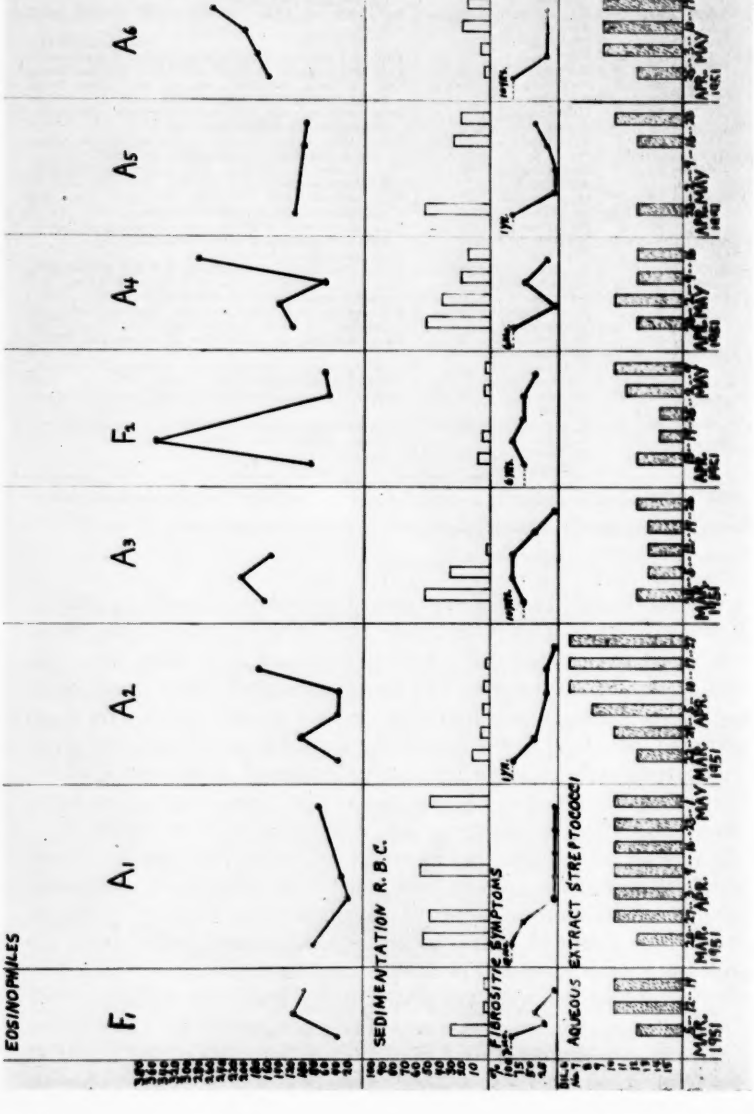
EOSINOPHILES
F1
A1
A2
A3
F2
A4
A5
A6
F3
SEDIMENTATION R.B.C.
FIBROSITIS SYMPTOMS
AQUEOUS EXTRACT STREPTOCOCCI
MAR. 1951
APR. MAY 1951

Chart I.

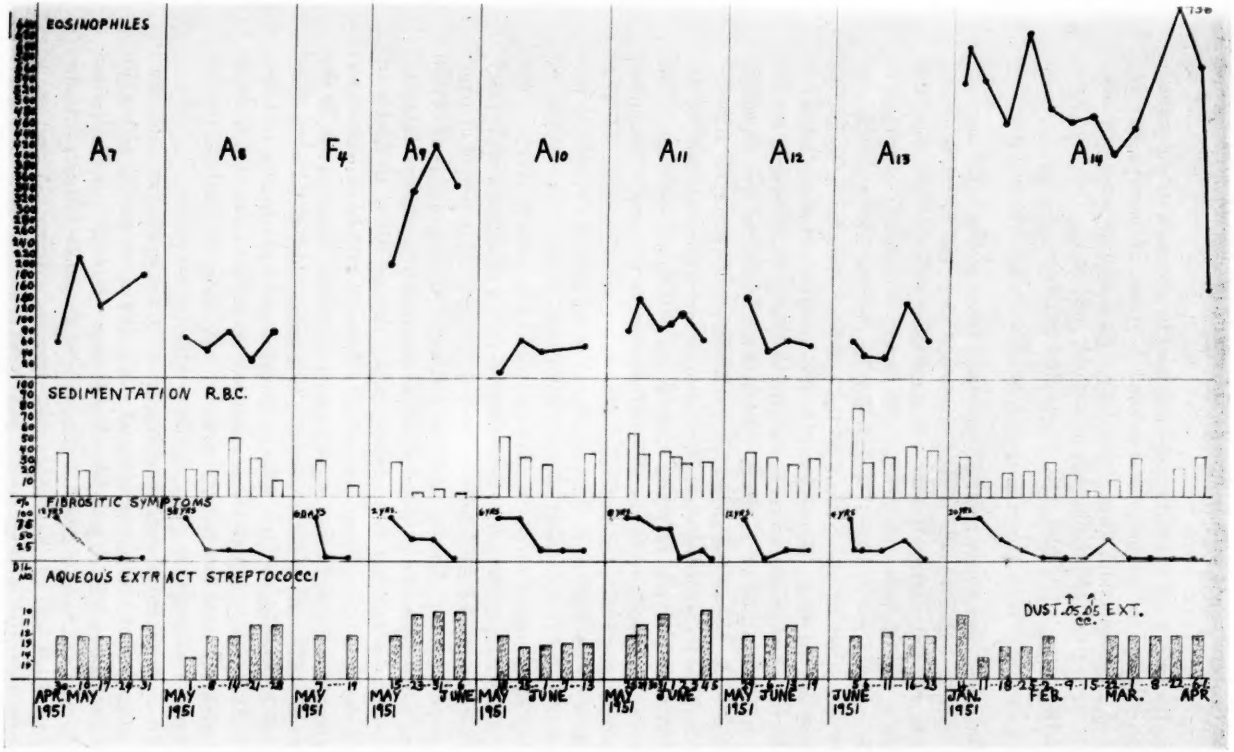

Chart II.

Charts I and II show the initial responses of eighteen patients with primary fibrositis and hypertrophic arthritis following injections of an aqueous extract of streptococci. Maintenance of improvement was accomplished by periodic injections. This is shown in records of A1 and the control case A14.

extract of house dust to which she was allergic was substituted, and prompt recession of symptoms after return to injections of the streptococcal extract.

Salicylates were not withheld and were used by fourteen of the patients but daily dosage in no instance exceeded 5 grains of aspirin and 2½ grains of acetophenetidin three times daily. As a routine procedure these patients were given 150 milligrams of ascorbic acid daily. This was withheld in two patients (A5 and A10) for control purposes.

DISCUSSION

In those instances where relief of symptoms followed the initial injection of antigen, it began usually within six hours after the intravenous and within twenty-four hours after the subcutaneous injections. Stiffness, pain on motion, and the persistent aching were among the earliest symptoms to be relieved. A sense of exhilaration following the first treatment was frequently described by the patient as the sudden lifting of a feeling of heaviness and tiredness. Improvement in the objective symptoms amounted to an increased range of motion in the affected parts; a decrease in tenderness; and a reduction of swelling. Reduction of swelling was especially noticeable in the bursae and about the digital joints in hypertrophic arthritis. Heberden's nodes sometimes lost their redness and tenderness but the decrease in their size was referable only to the soft tissue swellings. The new bone formations were not affected even after prolonged treatment.

The duration of the period of relief following a single injection of AES depends upon the size of the dose as related to the patient's needs. In our patients it varied from several days to two or three weeks. It is terminated suddenly by a relapse of the former symptoms but usually they are less severe. This relapse appears to be associated with a developing inadequacy of the former dose of AES since another injection of it, in proper amount again provides relief. Success with this method of treatment depends upon the nice adjustment of dosage of AES to the patient's requirements. In previous articles this has been discussed and dosage tables applicable to each of the rheumatic diseases provided.[6] These should be consulted for the recommended progression or regression of dosage in any series of injections of AES used in the treatment. It is suggested that 0.1 cc of dilution 10^{-12} be used as the first dose in fibrositis and hypertrophic arthritis since it most nearly represents a mean tolerated dose from which more accurate adjustments upward or downward may easily be made as the initial response indicates.

The relapse of clinical symptoms appears to be associated not with complete utilization of the former dose of AES, but more nearly with a 50 per cent utilization, which may be referred to as "half-life" of the former dose of AES. Follow-up doses at relapse time should be estimated on the assumption that half of the former dose remains effective. A previously published "half-life" table shows at a glance the amount of AES to be used at relapse time.[6]

If relief periods last from seven to fourteen days and the patient can be kept comfortable by an injection at these intervals, the dosage may be regarded as adequate early in the course. Later doses may be built up so as to provide continuous relief over periods of three to four weeks following single injections.

Ordinarily, primary fibrositis requires treatment over relatively short intervals, since there appears to be little tendency to recur. In the secondary fibrositis of hypertrophic arthritis, the symptoms continue to recur and treatment should be continued indefinitely at intervals of from two to four weeks.

Starting doses of AES which are too large may aggravate the symptoms during the first twenty-four hours, or longer (Cases A3 and F2) if gross overdosage has been used, so that any increase in pain, tenderness, swelling and resting stiffness during the first two days after an injection should be regarded as being due to too large a dose. There is more of a tendency to overdosage than to underdosage in the use of such a simple procedure so that at times in the earlier weeks in the course of treatment, the patient may show continuously an aggravated state of his symptoms over and above that low level achieved following the first few doses. This should always be interpreted as being due to overdosage, and a return to lower doses usually corrects the condition. The cumulative effects of doses repeated at weekly intervals, early in the course, may account for an aggravation of symptoms while on constant dosage. If the first dose is large enough to afford relief for a period of three weeks, and it is repeated at the end of one week, a build-up is accomplished and symptoms of overdosage may appear. It is therefore wise to instruct the patient to return for the second injection only after there has been a return of symptoms. In this manner both the dosage and the interval between treatments may be established promptly.

The aid which may be obtained from laboratory findings in adjusting dosage of AES in fibrositis is somewhat controversial because of the inconsistency of the results of the tests. An increase in the sedimentation rate of erythrocytes following the early injections of AES, if accompanied by no relief or by an aggravation of symptoms, is regarded as an indication of too large a dosage. In those cases of fibrositis which have an elevated sedimentation rate before treatment is started a prompt fall in the rate accompanies the relief of clinical symptoms following the early doses of AES. A persistently elevated sedimentation rate may be regarded as indicating too large a dosage throughout the series of injections. The direct eosinophile counts appear to be less closely related to the symptoms of fibrositis than is the sedimentation rate. There is usually an increase in the circulating eosinophiles following the initial injection of AES, but these counts level off with the subsequent injections of proper therapeutic amounts. We regard a persistent elevation of eosinophiles developing during treatment as an indication of overdosage of AES. A persistent second-

ary anemia during treatment is regarded as indication of too heavy a dosage schedule of AES.

SUMMARY

I. A desensitization technique which provides relief in primary fibrositis and in that secondary to hypertrophic arthritis is presented.

II. The long term periods of relief following single injections of an aqueous extract of streptococci suggests that these injections may influence the underlying causative factors of fibrositis.

CASE REPORTS

Patient F1.—A forty-four-year-old plasterer complained for the past three months of pain and stiffness in the elbows; pain and weakness in the arms. He had been unable to work for two months, and he had been treated by his local physician with penicillin and salicylates. Examined March 5, 1951, the patient was a normal appearing white man, seventy inches tall, and weighing 163 pounds. The pulse was regular at 84 per minute; the blood pressure 110/80 mm of mercury; and the temperature 99°F. Twenty teeth remained, all vital and in repair. A gingivitis of moderate grade was noted. The whole pharynx was acutely inflamed and an unusually long uvula was responsible for some pharyngeal irritation. Nothing unusual was found upon examination of the lungs, heart, nor abdomen. There was a slight contracture of the right elbow and tenderness over the epicondyles and over the tendon of the biceps. Forcing to complete extension or flexation of the right elbow caused pain. The left elbow was similarly involved but less severely. Both wrists were tender, but not swollen. The grip in each hand was weak but poorer in the right.

The diagnosis was primary fibrositis, infected pharynx and gingivitis. Chloromycetin, 250 mgs four times daily for the first four days was advised to aid in clearing up the pharynx. The initial injection of 0.1 cc of 10^{-12} dilution of the aqueous extract of streptococci was given subcutaneously at about noon and followed the next morning by relief to such an extent that the patient worked for a few hours—the first in two months. The symptoms returned and continued throughout the week. Upon his return visit, a larger dosage of the aqueous extract of streptococci (0.1 cc of 10^{-10} dilution) was given. Relief was complete and was maintained by weekly injections of this amount by his local physician who last observed the patient on May 17, 1951.

Patient A5.—A sixty-two-year-old housewife complained of pain, stiffness, tenderness, and deformity of the fingers; stiffness of the knees; pain in the right arm, and in the lumbosacral region, when seen on April 23, 1951. A toxic thyroid had been operated on fifteen years previously. Since 1950 she had been treated with injections of desoxycorticosterone and ascorbic acid, three times weekly for five weeks, two times weekly for the next five weeks and once weekly thereafter. The patient was a white woman sixty-four inches tall and weighed 157 pounds. The pulse was regular at 72; the blood pressure 130/80 mm of mercury; and the temperature 98.4° F. Only eight teeth were present and three of these were loose from recession of the gums and pyorrhea. An early cataract appeared in the right eye. There were Heberden's nodes on all fingers, and the proximal digital joints were enlarged, contracted and tender. The movements of the left shoulder were restricted and painful. There was tenderness over the right sacroiliac joint.

Diagnosis: Hypertrophic arthritis with deformities of the fingers; secondary fibrositis, right shoulder; pyorrhea; and cataract.

She was treated initially with the injection of 0.1 cc of 10^{-10} dilution of the aqueous extract of streptococci subcutaneously. Relief occurred overnight. During

the week following this visit she fell and fractured several ribs so that she did not return to the office until the twenty-third day after the first treatment. A relapse of symptoms occurred on the twentieth day. Relief was not as complete following the second injection, nor after the third seven days later using an increased dose, but the patient was later standardized on the initial dosage administered at fourteen-day intervals.

Patient A14, a seventy-year-old housewife, complained of acute tenderness, stiffness and pain in hands which had shown the deformities of hypertrophic arthritis for twenty years. She also was afflicted with an allergic bronchitis and intermittent attacks of asthma for which she had taken some injections of an extract of house dust. The patient was a pallid, white woman sixty-seven inches tall and weighing 143 pounds. The pulse was regular at 60, and the blood pressure 130/80 mm of mercury. The mucuous membranes of the nose were pale and dry. Both antra and both frontal sinuses were very clear upon transillumination. The tongue and sclera presented signs of a moderate deficiency of niacin and riboflavin. The hemoglobin reading was 70 gms per cent. No teeth were present and the tonsils were atrophic. Rhonchi and sonorous râles were general throughout the chest. There were active Heberden's nodes on all fingers and each thumb. The proximal digital joints were enlarged, showed flexion and deviation deformities, and were greatly limited in their movements. These joints were tender, red, and painful. There was tenderness over the left sacroiliac joint and the muscles to the left of the spine in the lumbar region were spastic. The diagnosis was hypertrophic arthritis, secondary fibrositis, allergic bronchitis, and B-complex deficiency. She was treated with therapeutic doses of multiple vitamins, intramuscular injections of liver extract, and diet. The first injection of streptococcal extract was larger than that regularly employed (0.1 cc dilution 10^{-10}) and was followed within twenty-four hours by aggravated soreness in the hands, headache, and nausea. After one week (0.1 cc of dilution 10^{-14}) a dose smaller than the usual starting dose was injected and relief began on the third day. Thereafter the dosage was gradually increased at weekly intervals. The clinical note of January 25 states that, "the patient has no pain and little tenderness. The soft tissue swelling has subsided and all redness is gone." Chart II shows that she was maintained at this low level of symptoms until dust extract injections were substituted for the streptococcal extract when a return of symptoms occurred. This improved after substitution of the streptococcal extract. The remarkably high level of circulating eosinophiles is perhaps related to her allergy to dust, and cannot be correlated with the fibrositic symptoms. The decided reduction of eosinophiles occurring at the end of the observation period can scarcely be related to the two injections of dust extract and were not accompanied by improvement in the bronchitis.

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TREATMENT OF RHEUMATIC DISEASES BY DESENSITIZATION WITH AN AQUEOUS EXTRACT OF STREPTOCOCCI

II. Rheumatic Fever, Chorea, and Rheumatic Carditis

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THERE is abundant evidence indicating that streptococci play a significant role in the etiology of rheumatic fever, yet the *modus operandi* in the production of this disease has not been found. Actual infection with streptococci produces pus in experimental and clinical experience but none appears in rheumatic fever or chorea. The tendency for rheumatic fever to develop from ten to fifteen days after an acute infection with hemolytic streptococci has directed attention to them as etiologic agents. The hemolytic property of these streptococci may be only incidental since subcutaneous injections of extracts of non-hemolytic streptococci have been followed by exacerbations of rheumatic fever[3] when overdosage was employed in its treatment. This suggests the hypothesis that the inflammatory lesions of rheumatic fever may be produced as allergic phenomena due to hypersensitiveness to an extractive of nonviable streptococci after their growth in a localized acute infection has been checked by the defenses of the body.

Effective methods of combating rheumatic fever are similar to those used in the treatment of allergic diseases. These may be stated in general terms as follows:

A. Removal of the patient from exposure to the sensitizing antigen, *e.g.*, residence in warm climates where streptococcal infections are not prevalent.

B. Dilution of the antigen when its elimination is not possible, *e.g.*, prophylaxis with sulfonamides or antibiotics; removal of foci of infection.

C. Reduction of tissue sensitiveness, through the use of salicylates, cortisone, corticotropin (ACTH), or hydrocortisone.

D. The use in treatment of a desensitizing technique with properly graduated and spaced doses of the sensitizing antigen which in rheumatic diseases appears to be an extractive of streptococci.

Much progress has been made in the prophylaxis and treatment of rheumatic fever through the development of categories A, B[1], and C[2]. Full advantage may be taken of each of these since their use does not appear to interfere with the simultaneous use of the desensitizing technique. The long-term results of the latter may eliminate the need of prolonged administration of sulfonamides or antibiotics for prophylaxis. Their availability for prompt suppression of acute upper respiratory infections due to

streptococci provides the physician with a method of inestimable value in the prevention of rheumatic fever. Salicylates should be used in the treatment of rheumatic fever during the acute febrile stages. The benefits from cortisone, corticotropin, and hydrocortisone in the acute stages have not been fully determined. We have not found them to be necessary in the interim treatment of rheumatic carditis or chorea by the desensitization methods.

THE AQUEOUS EXTRACT OF STREPTOCOCCI (AES)

A strain of *Streptococcus salivarius* (*Streptococcus cardioarthritidis*—Small) was used in preparing the antigen used for desensitization. The streptococci were grown in nutrient broth, washed free of the medium, and resuspended in normal saline in a concentration of 100 million per cubic centimeter. The suspension was shaken daily and kept in the refrigerator for an extraction period of seven days. The microorganisms were removed by filtration and the clear filtrate used as the undiluted antigen. From this filtrate a series of decimal dilutions in buffered neutral normal saline were prepared and designated, dilutions 10^{-1}; 10^{-2}; 10^{-3}; 10^{-4}; and so on to the extreme dilution 10^{-16}. In the treatment of rheumatic carditis and chorea, dilutions 10^{-16}, 10^{-15}, and 10^{-14} only are recommended. In many cases only the weakest of these three dilutions, 10^{-16}, is used.

We do not claim any immunologic specificity for this extract. Through the years, evidence has been obtained that extracts of other streptococci may be used with similar results. It is important to use a stock extract of a particular streptococcus because of the refinements needed in the adjustment of dosage. The stock extract maintained sterile and in the refrigerator may be used with consistent results for long periods of time.

The very minute doses used have been arrived at over a period of years, during which dosage reduction was stubbornly resisted but ultimately accepted as necessary if this form of treatment was to be successful in the rheumatic diseases. In another publication[5] the matter of very minute dosage was more fully discussed and other examples of comparable doses were presented. We believe that it is justifiable and important to use a form of treatment that has proved to be effective even though its exact mode of action in bringing about the beneficial results may not be completely understood.

TECHNIQUE OF DESENSITIZATION

The desensitization treatment of rheumatic carditis and of chorea may be more easily applied than that of fibrositis or rheumatoid arthritis, because from patient to patient, there appears to be less variation in the responses to a given dose of the streptococcus antigen, so that dosage becomes more nearly a matter of routine and the responses predictable. An examination of the progression of doses and the intervals recorded in

the tabulations in the three selected clinical reports will present this clearly. Although they differed greatly in severity, all three were started on similar doses of AES and at intervals of seven days. No change in either the dosage or the intervals was made in either of the three until very definite improvement occurred. In the most severe case this required ten weeks, in the others two and three weeks. Thereafter slight increases in dosage were made from time to time but perhaps of more practical importance was an increase of the intervals between treatments until the patients were on the perennial type of treatment of one injection per month.

Briefly stated then, our practice has been to give 0.05 cc of the 10^{-16} dilution of AES subcutaneously as a starting dose in each patient, and to repeat with this amount each week until there is a decided improvement in the clinical indicators—body weight, pulse, and temperature; and in the laboratory indicators—sedimentation rate of erythrocytes, leukocyte count, and hemoglobin. The dosage should not be increased until there is a tendency to gain in weight and until the sedimentation of erythrocytes approximates normal. Sixty per cent increments are safe when dosage is increased.* After the rheumatic process is adjudged to be quiescent, the intervals may be increased to ten days, then to fourteen, twenty-one, and finally to twenty-eight days. This latter constitutes the perennial type of treatment and may be kept up indefinitely. It may be undertaken with individual doses not larger than 0.1 cc of the 10^{-16} dilution of AES, and amounts larger than 0.15 to 0.25 cc of this dilution are seldom required as the injection at twenty-eight day intervals.

It is important to continue the injections at monthly intervals in the perennial phase of the treatment for at least a year after all signs of rheumatic activity have disappeared. Our practice has been to choose summer as the best season to discontinue the treatments. In some instances, after stopping for a summer, the injections were started again in the autumn and continued throughout another winter.

In the event of an acute streptococcal infection, we have reverted to the 0.05 cc of the 10^{-16} dilution of AES at weekly intervals until the danger of an exacerbation of the rheumatic process is adjudged to have passed. We now use antibiotics and sulfonamides to overcome these infections promptly thereby providing double assurance against such exacerbations. These drugs were not available when treatment was begun in one of the patients whose records are presented, but were used on another (Case 1) when he developed an acute tonsillitis.

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*Formerly we used this progression of dosage—0.05 cc; 0.1 cc; 0.15 cc; 0.2 cc; 0.25 cc; and 0.35 cc. We now use the constant increment progression (4)—0.06 cc; 0.1 cc; 0.16 cc; 0.26 cc; 0.42 cc, etc., in which each new dose is equal to the sum of the last two.

DISCUSSION

The physician will most likely court failure with this treatment if the recommendations regarding dosage are exceeded. An attempt to hurry a favorable response by spacing the doses at shorter intervals than those recommended is also fraught with danger of failure. These precautions are added because in our experience failure to adhere strictly to these two directions have so frequently resulted in failures for those physicians attempting this treatment for the first time.

Restraint in avoiding overdosage may be observed in the record of Patient 1. The weakest dilution of AES, 10^{-16}, was used throughout treatment periods totaling two and one-half years, and the largest single dose used was 0.15 cc of this dilution. The intervals were increased as the condition improved until the perennial type of treatment was maintained on this amount injected every twenty-eight days.

The need for patience is emphasized in the early record of Case 2 when a weekly dose of 0.05 cc of dilution 10^{-16} AES was maintained for ten weeks before the rheumatic activity quieted sufficiently to venture the use of larger doses. Thereafter, for a period of three and one-half years, with a heart irreparably damaged by repeated acute exacerbations of rheumatic fever, the patient was maintained at his work without sign of further exacerbation on the perennial type of treatment with doses of dilution 10^{-14} AES.

In the tabulated record of Case 3 is illustrated the responsiveness of the peripheral arthritic and fibrositic symptoms of rheumatic fever to the desensitization treatment with AES. After very prompt response the early doubling of dosage of AES was followed by a return of pain and stiffness, and also by the appearance for the first and only time of edema of the legs which disappeared without treatment as the painful symptoms subsided.

Case 1.—A thirteen-year-old boy was brought to the office in October, 1948. His medical history included measles, mumps, and chickenpox. The father and an aunt had had rheumatic fever but none of eight brothers and sisters had suffered such attacks. His initial attack of rheumatic fever occurred in May, 1948, and confined him to bed for two months. One week before coming to the office he had started to school and choreic movements were noted for the first time, making it difficult to hold pencil or books..

Physical examination.—The patient was a pallid white boy fifty-nine inches tall and weighing eighty-eight pounds. The pulse was regular at 88 and the temperature 99.0° F. The tonsils were large and hyperemic. Normal resonance was present throughout the chest. The cardiac impulse was diffuse and noted in the fifth and sixth interspaces 8.5 cm from the midline. A thrill was present over the apical region and also a loud systolic murmur which was transmitted well into the left axilla. A soft systolic murmur was noted over the base of the heart. All joints were free of arthritis. There were no subcutaneous nodules. Both hands and arms showed active purposeless movements. Co-ordination was impaired. Speech was not affected.

TABLE I.

Patient 1	Dosage AES Dil. 10^{-16} cc	Intervals Days	Sed. rbc. mm§	Wbc.	Hgb. Gms. %	Pulse	Body Wt. Lbs.
10-27 to 11-26-48	0.05	7	42	5,300	81	84	88
11-26 to 1-17-49	0.1	7	8	6,300	88	78	91
1-17 to 3- 5-49	0.1	14	6		83	78	92
3- 5 to 4- 2	0.15	14	9		85	72	95
4- 2 to 5-21	0.15	14	8			72	96
5-21 to 9-15	0.15	21	21*		80	72	100
9-15 to 12- 3	0.15	21	9	7,300	82	72	113
12- 3 to 3- 4-50	0.15	21	10	6,400		70	123
3- 4 to 5-13	0.15	28	9	6,400	92	78	131
5-13 to 9- 9	none	—	10	5,200		72	132
9- 9 to 12-16	0.1	28	4	5,600	82	86	129
12-16 to 3-17-51	0.1	28	7	5,600	90	72	147
3-17 to 5-11	0.1	28	12	5,900	90	76	152
5-11 to 8- 9	none	—				—	146
8- 9 to 1-24-52	none	—	10		94	80	147
1-24 to 10-25	none	—	12	6,500	91	68	132
10-25 to 1-23-53	none	—	2		96	80	133
1-23	0.05	—	25†	7,400	93	84	133
1-30	0.05	7				80	132
2-13 to 3-14	0.05	14	11			84	—
3-14 to 3-27	0.05	13	4	4,200‡	73	76	—
3-27 to 4-10	0.05	14	12			76	—
4-10 to 4-23	0.05	13	7		80	80	136
4-23 to 5- 9	0.05	16	17			76	135
5- 9 to 5-23	0.05	14	6			96	139
5-23 to 9- 9	none	—	8		91	78	138

*Severe ivy poison.
†Acute tonsillitis suppressed with penicillin, followed by sulfadiazine 0.5 grams twice daily.
‡Intolerance to sulfadiazine. Stopped 3-17-53.
§All sedimentation tests by Westergren Method.

Diagnosis.—Rheumatic carditis and chorea.

Treatment.—The general treatment of rest, tonics, and mild sedation set up by the referring physician were not disturbed. In addition a course of injections of the aqueous extract of streptococci (AES) was advised and administered by his family physician. We saw the patient from time to time and directed dosage.

After the third injection the choreic movements had disappeared and the sedimentation of erythrocytes had returned to normal. The boy was continued in school for half-days during November and thereafter full time throughout the 1948-49 school year.

We have been privileged to follow this patient for five years during which time the only significant illness has been an attack of acute tonsillitis in January, 1953. The tabulation below covers this and shows the manner of resuming the injections of the aqueous extract of streptococci in this acute illness twenty months after it had been discontinued. The acute phase of the tonsillitis was suppressed with penicillin, and sulfadiazine was used prophylactically for about seven weeks until symptoms of an intolerance developed. There was no indication of an exacerbation of the rheumatic carditis following the tonsillitis.

On October 9, 1953, the heart continued to present a thrill at the apex and a loud systolic murmur without departure from adequate cardiac function.

Case 2.—A twenty-one-year-old white man was first seen on July 2, 1937. His mother had died at age of thirty years of a rheumatic heart. The date of his first attack of rheumatic fever could not be definitely established but it apparently had occurred in very early childhood since an operation for adhesive pericarditis had been performed when he was seven years old. He recalled a prolonged attack with joint involvements at the age of sixteen years and the most recent exacerbation began three months ago. This had confined him to bed and the house until two weeks ago.

TABLE II.

Dates	Dosage AES cc 10^{-16}	Intervals in Days	Sed. rbc. mm	Wbc.	Hgb.	Pulse	Body Wt. Lbs.
1937							
7- 2 to 9- 9	0.05	7	100	7,200	56	112	121
9- 9 to 9-27	0.1	7	40	4,600	75	102	124
9-27 to 10-14	0.2 10^{-15}	7	45	9,600		108	127
10-14 to 11-13	0.05	7	22	6,800		90	129
11-13 to 12- 9	0.1	7	12	6,100		96	133
12- 9 to 3-28-38	0.15	10 to 14	8			90	133
1938							
3-28 to 5- 9	0.35 10^{-14}	14	5	6,700		84	137
5- 9*-38	0.1	14	8	5,300	88	84	143
2-14-42	0.1	(14,21,28)	5	6,300	91	84	140

*During a period of slightly more than three and a half years (May 9, 1938 to February 14, 1942), the dosage of AES was maintained at 0.1 cc of dilution 10^{-14} but the intervals were lengthened from fourteen to twenty-one and finally to twenty-eight days. Twenty-five observations were made during this period. In none of them were indications of an exacerbation of the rheumatic process found. The notations at the beginning and end of this period are typical of the clinical and laboratory findings throughout. Twelve days after the last observations, on February 26, 1942, while in his usual state of health, he suddenly collapsed and died before medical aid could be summoned. The exact cause of death was not determined. It might reasonably be presumed that embolism or thrombosis was the cause of his sudden death.

Physical examination.—The patient was a pallid white man showing throbbing arteries in the neck and considerable dyspnea. The pulse was of the Corrigan type, and was regular at 112 per minute. Systolic blood pressure was 140 mm of mercury. The diastolic could not be determined because of a constant bruit over the cubital space. The temperature was 98.0° F. There was a long operative scar over the costosternal cartilages to the left of the midline. The cardiac apex was against the left wall of the thorax. There was a diastolic-systolic murmur at the base and a systolic murmur at the apex of the heart. Cardiac dullness was easily percussed and was about 16 cm in width. Peripheral signs of aortic regurgitation were very apparent. There were no râles at the pulmonary bases and there was no edema of the legs. The hemoglobin was 8.8 grams and sedimentation of erythrocytes amounted to 100 mm in one hour. The patient had been on digitalis and it was yet very apparent that there was little cardiac reserve.

Diagnosis.—Rheumatic carditis; *cor bovinum;* aortic and mitral valvular lesions; adhesive pericarditis; and secondary anemia.

Treatment.—Rest in bed for a month. This was followed by another month's rest at the seashore, after which he was able to return to his work as a laboratory technician. A course of injections of the aqueous extract of streptococci (AES) was outlined and administered by his family physician. The summary in Table II shows some of the details.

Case 3.—A thirty-seven-year-old nun came to the office in September, 1949, complaining of tiredness, stiffness and general aching. In childhood she had measles, chicken-pox and scarlet fever. She had frequent attacks of tonsillitis prior to a tonsillectomy in 1939. One sister had rheumatic fever but the patient had never had a typical attack.

The present illness began with stiffness in the knees and feet five weeks previously. The hands, elbows, shoulders, ankles, and neck became involved in succession. As

new involvements appeared former ones cleared up. The patient continued her teaching but required assistance in dressing in the morning. She became less stiff after moving about and after taking aspirin but was exhausted at the end of the day.

Physical Examination.—The patient was slightly sallow, sixty-one inches tall, weighed 126 pounds. The temperature was 99.2° F. Ears, nose, and sinuses were free of infection. No tonsillar tissue remained and the pharynx was not hyperemic. Fourteen teeth remained, all clear by x-ray examination. There were normal findings over the lungs. The cardiac impulse was in the fifth interspace 12 cm from the midline. A systolic murmur at the apex was transmitted outward to the mid-axillary line. A soft systolic murmur at the base appeared loudest over mid-sternum at the level of the second interspace. There were no thrills. The rhythm was regular, and the rate 84 per minute.

No swelling nor tenderness appeared about any of the large joints of the extremities. Slight swellings, redness, and acute tenderness were noted about three proximal digital joints. The second and third right metatarsophalangeal joints were tender but not reddened. The patient moved the shoulders, knees, and neck stiffly but no arthritic localizations were apparent.

The hemoglobin was 90 grams per cent; the erythrocytes 4,300,000 per cu mm; and the leukocytes 4,800 per cu mm. Polymorphonuclears 61 per cent; lymphocytes 38 per cent and eosinophiles 1 per cent. Urea nitrogen was 9 mgms; uric acid 2 mgms and sugar 82 mgms per 100 cc of blood. The sedimentation of erythrocytes amounted to 38 mm in one hour. The Kahn test was negative.

The urine tests were normal.

Diagnosis.—Rheumatic carditis with low-grade peripheral involvements of joints and muscles.

Treatment.—The patient was allowed to continue her regular work and to use aspirin, as before, when needed. The aqueous extract of streptococci (AES) was begun by subcutaneous injection and continued as follows:

TABLE III.

Date 1949	Dose AES, 10^{-10} cc	Intervals in Days	Sed. rbc. mm	Pulse	Body Wt. Lbs.
9-21	0.05		38	80	126
9-29	0.05	8	30	72	128
10- 6	0.1	7	7	72	128
10-13	0.1	7		72	128
10-27	0.2	14		78	130
11-10	0.1	14	12	84	132

Following the first injection the patient suffered from headache for three consecutive days. After the second injection there were acute exacerbations in one hand on the fourth day, and in the left ankle on the seventh day. On the sixth day, moderate edema of the feet and legs was noted. The intervals following the third and fourth injections were uneventful and practically without pain. The larger fifth injection was followed by tenderness and general soreness for two days. No subjective symptoms have appeared since. The swellings, redness, and tenderness about the digital joints have disappeared. A prompt return to normal of the sedimentation of erythrocytes paralleled the clinical improvement. This patient was last observed on June 11, 1953.

SUMMARY

A method for the effective desensitization treatment of rheumatic carditis and chorea is presented.

The preparation of an aqueous extract of streptococci for use as antigen in this treatment is described.

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101 South 39th Street

NEW SCHERING AWARD WINNERS ANNOUNCED

Medical authorities in their special fields have selected the three winning papers in the 1953 Schering Award competition for medical students, according to an announcement by Dr. George Babcock, chairman of the Award Committee. A $500 prize goes to the winner for each of three topics.

The three topics and prize winners for the best essays were: "New Concepts in the Treatment of Peptic Ulcer" by Irving Paul Pollack, sophomore at the University of Maryland College of Medicine; "Hormone Therapy of the Degenerative Diseases," by Frank Edward Young, sophomore at the State University of New York at Syracuse College of Medicine; and "Antihistaminic Treatment of Upper Respiratory Allergies and Infections," by George Richard Pieper, junior at the University of Utah College of Medicine.

Fulfilling the major objective of the Schering Award, which is to encourage research and reporting by medical students, the three award-winning papers of 1952 have recently been published in medical journals.

The Journal of the American Geriatrics Society (February 1954), published Edward Allen Jones' paper, "Steroid Hormones in Geriatrics."

California Medicine (December 1953) published the paper by William H. Spencer, on "Chemotherapy of the Eye."

The Journal of the Student American Medical Association (March, 1954) published the paper by Seymour Cohen, M.D., "Topical Uses of Antihistamines," dealing with skin allergies.

Each year, Schering Corporation, pharmaceutical manufacturer of Bloomfield, New Jersey, grants $500 awards for the best paper on each of three subjects and three $250 second prizes.

SENSITIVITY REACTIONS NOTED IN IMMUNIZATION WITH INFLUENZA VIRUS VACCINE

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EARLY in the use of influenza virus vaccine, it was evident that it was of value, but undesirable local and constitutional reactions were being observed. In 1948 Lienke[6] reported that fewer systemic reactions are encountered with calcium phosphate adsorbed vaccine administered in the recommended dosage, possibly due to the repository effect produced by the calcium phosphate and the consequent slow adsorption of antigen. Several years earlier Chambers[1] had stated that protamine precipitated vaccine, like the calcium phosphate absorbed vaccine, apparently contains less allergenic substance than the vaccine prepared by erythrocyte adsorption. Stanly[15] wrote that vaccine prepared by centrifugation is virtually free of substances causing allergic reactions. Ratner and Untracht[9] emphasized the importance of egg sensitivity. They cited several allergic reactions in patients who gave clinical histories of egg sensitivities and recommended that all patients be tested with 0.02 cc of the undiluted vaccine. Curphy[2] has reported a fatal hemorrhagic allergic reaction to influenza vaccine in a small child. About six hours after the inoculation the temperature rose to 109° F. and the patient soon died. The autopsy did not show the typical picture of anaphylaxis. The lungs revealed an interstitial pneumonia, which resembled the changes seen in virus pneumonia. Curphy stated that the child might have had a virus infection at the time of the inoculation, although it was apparently well at that time. He also stated that another child, injected at the same time, had a reaction with a rise in temperature to 102° F. Salk[13] has stated that the severity of reactions following inoculations with influenza virus was related to the quantity of the virus introduced and was not due to impurities.

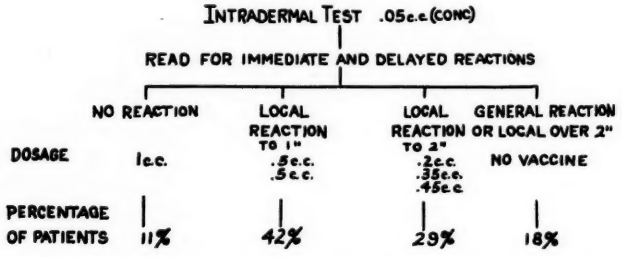
Most of the Commercial Influenza Vaccines contain four strains of virus, PR8 (type A), FMI (type A), Cuppett (type A) and Lee (type B) in an aqueous medium. The strains are grown and harvested from the allantoic fluid of chick embryos and the vaccines are standardized by the official method of the National Institute of Health. After concentration, the viruses are inactivated by either formaldehyde or by irradiation. A preservative of Thimerosal, sodium ethyl mercuric thiosalicylate or other chemical is added.

A lecture, given in part, at the Saint Francis Hospital Scientific Day, April 11, 1953.

From the Department of Allergy, Saint Francis Hospital, Pittsburgh, Pennsylvania, with the co-operation of John R. Orie, M.D., Miss Doris Johnson and Miss Marie Fitz.

TABLE I.

SCHEDULE OF IMMUNIZATION WITH INFLUENZA VIRUS VACCINE



Sensitivity Reaction Noted in Immunization with Influenza Virus Vaccine.

In January, 1949, we initiated studies of influenza virus vaccine immunization on allergic patients from the Saint Francis Allergy Clinic and from a private allergy practice. The study was carried out first on a group of one hundred and fifty patients who had been receiving immunizing injections over a long period of time for upper and/or lower respiratory symptoms. Later a second study was done on a group of one thousand individuals. Both groups consisted of men, women and children.

STUDIES ON GROUP I

All the patients in this group were skin tested for sensitivity to chicken, egg and feathers and were found to be negative and none of them were clinically sensitive to fowl in any form. Each patient was given an initial test dose of 0.05 cc of the influenza virus vaccine (concentrate) intradermally. The patients were observed for reactions after twenty minutes, one day, two days, three days and one week. The results are given in Table I. As may be seen from this table, the immediate reactions were few, and slight in degree. This was to be expected as the reactors to chicken had been eliminated. Eleven per cent of the patients gave no reactions, forty-two per cent gave a delayed local reaction not exceeding one inch, twenty-nine per cent gave a delayed local reaction between one and two inches and a surprising eighteen per cent showed delayed local reactions over two inches in diameter and/or delayed constitutional reactions. Both the local and general reactions began about twenty-four to thirty-six hours after the injection and reached a peak in three to four days. The majority of the general reactions were respiratory in nature, with rise in temperature and malaise also frequently noted. The symptoms varied greatly in severity and lasted from a few hours to many days. A few patients were incapacitated and were confined in bed from five to seven days. A few of these had temperatures ranging to 104° F. The

general reactions in these patients appeared similar to those of acute attacks of type A influenza. In some patients these reactions were accompanied by gastrointestinal symptoms mainly diarrhea. In these patients the reactions resembled those of type B influenza.

On the basis of these preliminary observations a schedule of immunization was adopted as indicated in the table. Following a reaction to a test dose or an immunization dose, the next inoculation was not given until the previous reaction had almost completely subsided. If at any time during the immunization period any large local or constitutional reactions were noted, the vaccine was discontinued. By means of this procedure about five per cent of the patients were eliminated from the study.

Salk[12] suggested that the antibody titer after initial vaccination might remain at a protective level for about six months. With this in mind we decided to give the patients, who completed the initial schedule, 0.5 cc of the vaccine every six months as a booster dose. We realized, of course, that this dosage might be too large for some patients, but a number of them received two or three booster treatments before developing a large local reaction or general symptoms. About twenty per cent of the patients developed acute influenza symptoms in spite of the inoculations. Twenty-five per cent of these attacks occurred soon after an inoculation but the remainder of these acute symptoms occurred in from four to six months following the initial inoculations or a booster dose. Obviously, either these individuals had not developed sufficient protection, the protection did not last six months after inoculations, or else the virus producing the infection had not been included in the vaccine that we used. In studies on poliomyelitis vaccine, Saslaw[14] found that, although antibodies induced by immunization were still present four and one-half months later, it could not be predicted how much longer they would persist. We concluded that the booster dose of influenza vaccine would have to be smaller and that the doses would have to be given at closer intervals.

STUDIES ON GROUP II

After the foregoing studies were completed a second group of allergic patients was selected, consisting of one thousand individuals. This time patients who gave positive skin tests to chicken, egg or feathers were not excluded from the study, unless they gave exceedingly strong reactions with dilute extracts. However, all patients that were clinically sensitive to fowl were again excluded. Many individuals from Group I, who had shown rather large local reactions to the 0.05 cc intradermal injections of the influenza virus vaccine were included. The initial intradermal test dose used with the patients in Group II was 0.05 cc of a one to one hundred dilution of the concentrated vaccine. If there was no immediate or delayed reaction, the patient was tested with 0.05 cc of a one to ten

dilution, and if again no reaction ensued, with 0.05 cc of the concentrated vaccine. If at any time a large local reaction or general symptoms were noted, the vaccine was discontinued. No general reactions were encountered with the one to one hundred dilution but several patients developed significant symptoms soon after the one to one hundred was raised to 0.2 cc, 0.4 cc or 0.6 cc during the course of the treatment series. A large number of persons who had reacted strongly in the studies on Group I sooner or later reacted in this study. Only a few slight local reactions of the immediate type were seen. Again, the local and general reactions encountered were of the delayed type. The interval between inoculations for both testing and treatment was one week.

In this second group a total of 1.0 cc of the concentrated vaccine in divided dosage had finally been given to those patients on whom the treatment was completed. Therefore, over a period of several months many patients had received a large number of inoculations. This was not much of a problem to the patients or us as the virus vaccine was being given along with other specific antigens. The entire period of inoculation was shortened if the patient did not react to the one to one hundred dilution or reacted slightly or not at all to the one to ten. The initial dose then consisted of the one to ten or the concentrated solution.

This second group of patients was given intradermally 0.1 cc of the vaccine every three to four months. This seemed adequate to keep the protection at a high level. With this relatively small dosage a few individuals experienced large local delayed reactions or general symptoms. When a reaction did occur it might follow the first booster injection or any of the following ones. Immunization of these cases was then stopped.

In our studies it was noted several times that a vaccinated patient might not get influenza, while four or five unvaccinated members of the same family in the same house were suffering from acute influenza symptoms.

Three types of sensitivity reactions may be seen when inoculations with influenza virus vaccine are given:

1. *Reactions due to fowl sensitivity.* This reaction was almost completely eliminated by excluding all patients known to be clinically sensitive to fowl.

2. *Reactions to the preservative or inactivator chemicals in the vaccine menstruum.* Formalin or mercurial compounds are the main sensitizing chemicals to be considered in this category. We encountered two cases of scaly dermatosis of the face in patients known to be sensitive to formalin. This form of sensitivity could be especially important in the immunization programs of large groups of industrial workers.

3. *The delayed reactions.* These reactions, whether local or general, were the induced type of sensitivity. Thus, they could be predicted to

occur in the normal population but not as frequently as they were seen in the allergic patients studied.

These studies suggested that, if the persons clinically sensitive to fowl were eliminated, it was safe to begin immunization with the one to one hundred dilution of the A and B influenza virus vaccine in any patient whether allergic or non-allergic and whether adult or child. This is our present method and the dosage is raised through the three dilutions until 1.0 cc total vaccine (concentrate) has been given. The injections are stopped at any level when untoward local or general reactions are observed. Using this slow schedule, a large percentage of patients will complete the immunization without difficulty.

DISCUSSION

Francis, Herst, Magill, Salk and others[4,5,7,8,10,11] have written on immunization against influenza in epidemics with specific virus vaccine and the protection which was shown. With the aqueous vaccine, a conservative long program of immunization is most satisfactory to diminish the frequency of delayed reactions. It would appear unsound in large industrial immunization programs to give 1.0 cc of the concentrated vaccine without at least testing intradermally with 0.05 cc as a preliminary procedure. More effective vaccines are being developed. These newer ones may further reduce reactions, increase protection to many more types of virus, and lengthen the time between booster injections. Salk[12] has recently reported a vaccine emulsified in a mineral oil with which higher titres of antibodies that persisted for a long time were observed. His study, plus others,[3] are ever increasing our knowledge of the influenza virus and bringing closer at hand a better and safer vaccine.

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121 University Place

ELEVENTH ANNUAL CONGRESS IN CHICAGO, 1955

Surely you will want to attend the Eleventh Annual Congress of the College, which will be held at the Hotel Morrison, Chicago, Illinois, April 25-30, 1955. Please make a note on your desk calendar now to attend what will probably be the largest convention ever held in the history of the College. Fortunately, previous far-sighted Regents, appreciating the greatly increased number of medical conventions, and endeavoring to avoid conflict with other medical groups which may have a program on allergy, have ruled that the Congress should be held in Chicago every other year. There are a number of medical societies that have established Chicago as their permanent convention address. This saves much effort when planning an instructional course and scientific and technical exhibits. The hotels there have every facility for holding large conventions, with adequate projection equipment, proper ventilation, et cetera. The time for meetings must now be arranged at least five years ahead because of the many bookings made by the larger hotels in demand for conventions. An over-all plan of holding a convention on the Eastern seaboard, or in an adjacent area, and again in the middle South, middle United States and West Coast, every other year is no more than fair to the members of the College.

The many details of arranging an instructional course and developing the annual conventions are in the hands of a group with many years of experience. We have appreciated the co-operation of the membership in the past, and hope that you definitely plan to attend the Chicago meeting next April. The new Morrison Hotel has been completely remodeled, and the management is prepared to take care of a large attendance, with proper entertainment facilities, and arrangements for an unlimited number of technical and scientific exhibits. If you plan on a scientific exhibit, start now to make arrangements. The Program Committee is now meeting to make preliminary plans for the next instructional course and scientific session.

VASOMOTOR RHINITIS AND BRONCHIAL ASTHMA DUE TO LOCUST BEAN GUM DUST

ISIDORE MECHANECK, M.D.
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FOR the past twenty years reports of sensitivity to commercial gums have appeared from time to time. Vasomotor rhinitis and bronchial asthma are the most frequent symptoms produced by inhalation of the dust. Occasionally direct contact produces dermatitis and ingestion produces gastrointestinal symptoms, urticaria and angioneurotic edema. Most of the reported cases have occurred through occupational contact.

Spielman and Baldwin[7] described a case of vasomotor rhinitis and bronchial asthma due to Acacia (gum arabic) sensitivity in a plaster molder. Direct tests and passive transfer tests were positive.

Feinberg and Schoenkerman,[3] Bohner, Sheldon and Trevis[1] and King[6] described cases of bronchial asthma due to Gum Acacia.

Bullen,[2] Figley,[4] Feinberg and Schoenkerman,[3] also described cases of vasomotor rhinitis, urticaria and bronchial asthma due to Karaya Gum. Most cases were due to contact with the gum in hair-waving lotions but other sources were laxatives, dentures and denture adhesive powders.

H. H. Gelfand[5] in his extensive article on the allergenic properties of vegetable gums reports a case of bronchial asthma due to Tragacanth Gum.

The case described below is, I believe, the first case of bronchial asthma and vasomotor rhinitis caused by sensitivity to Locust Bean Gum. This gum also goes under many other names, Crab Gum, Carob Seed Gum, St. John's Bread, Swine's Bread, Gum Gatto, Gum Hero, Sanda Gum, Lakoe Gum, Luposol, Rubigum, Tragon and Tragasol.

The locust bean is a hemicellulose. This embraces a group of substances which are closely related chemically and which are contained in the seeds and fruits of various plants. The cellular tissue of these plants consists largely of products intimately associated with cellulose and chemically allied thereto.

The hemicellulose materials which find commercial application are Locust Bean Gum, Locust Kernel Gum, Guar and extracts of seeds such as those of Quince, Psyllium, Flax; as well as Lichens such as Iceland Moss.

Locust Bean Gum is imported from Great Britain, France and the Mediterranean Area. The Carob or Locust Bean tree, Ceratonea Saligna L., is widely cultivated in Southern Europe, on various islands of the Mediterranean Sea and in Northern Africa. It is used commercially as a thickener in ice cream mixtures, in printing pastes, in sizing and in finishing white and printed fabrics; as a thickener in printing with diazo solutions,

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acid resists and acid colors in wool and silk; for printing cotton draperies and dress goods; and in the application of Vat Colors by spraying and in water-proofing.

Case History: J. W., age 38—male patient was in apparent good health until May, 1952. From age eight to fourteen he had attacks of allergic rhinitis and bronchial asthma from the middle of August until about the end of September. This condition was diagnosed as hay fever. The only treatment given at that time was Adrenalin injections for the acute attacks. He had no symptoms after age fourteen until the present.

Family History: An older sister had a skin rash from eating strawberries and bananas.

Present History: Patient has been employed as a chemist in a Long Island City Plant since April, 1951. In May, 1952, while in the plant, the patient began to have attacks of sneezing, rhinitis, profuse nasal discharge and blocking of the nose. The attacks were soon followed by congestion in the chest, difficulty in breathing, wheezing and cough. The attacks were mild at first but gradually increased in intensity until on August 18, 1952, an attack was so severe that the patient came to my office for relief. An injection of Adrenalin gave relief.

In view of the previous history and the fact that it was the hay fever season, it was first thought that the patient had a recurrence of his hay fever. He was given an antihistamine and Tedral tablets.

Intradermal skin tests for the common inhalants were performed and the following positives were obtained:

House Dust	1 plus
Plantain	1 plus
Timothy	1 plus
Ragweed	2 plus

On August 25, 1952, he had another severe attack of bronchial asthma. On further investigation it was discovered that:

1. He experienced no difficulty outside of the plant and outside of working hours. He had no symptoms on weekends.

2. The only time he experienced difficulty in the plant was when certain gums, namely Locust Bean and Guar, were being processed. The material is passed from one floor to another through a chute which is not airtight, and workers are exposed to the dust of the gums. The chute passed near the laboratory where the patient worked.

The patient was asked to bring extracts of the gums and he was skin tested with a 1 per cent solution. There was a positive reaction to Locust Bean Gum and the wheal formed became markedly pruritic. The reaction to Guar Gum was negative.

The patient then confirmed the fact that only when Locust Bean Gum was processed did he have difficulty. He was advised to wear a face mask while working.

An autogenous extract 1 per cent solution of Locust Bean Gum was prepared by the Center Laboratory of New York and Desenitization was begun on September 10, 1952, beginning with 0.1 cc of 1:10,000 dilution and increasing gradually. On one occasion when 0.1 cc of 1:100 dilution was given the patient had an attack of bronchial asthma. This was controlled with Adrenalin. The last dose given was 1 cc of 1 per cent dilution on October 31, 1952. The patient showed no improvement.

As other gums were being processed in small amounts, the patient was skin tested with the following results:

Gum Tragacanth	———
Gum Arabic	1 plus
Gum Karaya	———
Gum Tara	———

Passive transfer tests on October 31, 1952, gave a positive reaction to Locust Bean Gum. The control was negative.

The patient was referred to Dr. Joseph Harkavy by the insurance company for consultation since it was an occupational ailment. Dr. Harkavy confirmed the positive skin tests on the patient and also performed skin tests on several clinic patients and obtained some positives. The significance of this is not known.

On November 15, 1952, Dr. Harkavy sprayed the Locust Bean extract into the patient's nostrils and he immediately developed severe sneezing, rhinitis and a choked-up sensation. The patient's nose was washed out thoroughly and an injection of Adrenalin was given.

Attempts at desensitization with nasal and throat spraying with a nebulizer was begun with 1:10,000 dilution on November 22, 1952. The spraying was done three times weekly, gradually increasing the concentration of the solution. At 1:40 concentration, the patient developed severe rhinitis and asthma. This method of desensitization was continued until the end of January, 1953. The patient showed no improvement and still developed attacks of asthma and rhinitis on exposure to Locust Bean Gum Dust. He was advised that there were only two alternatives, either that he resign his position or work in a laboratory where the incoming air is filtered and air-conditioned.

A York model three and one-half ton air conditioner and filter was installed in the laboratory in June, 1953. This unit brings in 1800 cubic feet of air a minute. The air is filtered through two series of fiber glass.

While the patient works in the air-conditioned laboratory he has no symptoms. On exposure to Locust Bean Gum Dust there is still a recurrence of the symptoms.

SUMMARY

1. A case of sensitivity to Locust Bean Gum is reported.

2. Gum sensitivity is an occupational hazard for predisposed individuals.

3. As reported by many, a relatively long period of exposure is necessary before a predisposed individual manifests clinical symptoms (in this case more than one year).

4. Desensitization to gums is difficult and not too successful.

5. Spontaneous tolerance may be developed.

6. Several methods of diagnosis of sensitivity to a suspected material as well as different methods of attempts of desensitization are presented.

7. Removal of the individual from the source of sensitivity or removal of the allergen by filtration and air-conditioning is frequently the only logical treatment.

8. The vegetable gums may play a greater role in allergenic conditions than is suspected at present.

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89-34 Van Wyck Expressway

FUTURE ISSUES

The May-June ANNALS OF ALLERGY will contain the Convention Echoes of the recent very successful Decennial Congress of the College held at Miami Beach, Florida. It will announce the officers elected, the new Board of Regents, changes adopted in the By-Laws, reports of committees, and other interesting news. Be sure to read these Proceedings carefully, so that you may familiarize yourselves with the present activities of the College.

The June *Quarterly Review of Allergy and Applied Immunology* will contain a feature article by Dr. M. Rocha e Silva, Department of Biochemistry and Pharmacodynamics, Instituto Biologico, São Paulo, Brazil, on "Anaphylatoxin and Histamine Release." There will also be a preliminary report by the editor reviewing the fluid and electrolyte metabolism with a consideration of its application to allergic diseases.

WANTED

An eminent research scientist is interested in securing a qualified allergist who is capable of carrying out further researches in allergy. Please inquire at College headquarters, 401 LaSalle Building, Minneapolis, Minnesota, and give qualifications.

ALLERGIC TENSION-FATIGUE IN CHILDREN

FREDERIC SPEER, M.D., F.A.C.A.
Kansas City, Kansas

IT HAS long been known that a characteristic pattern of behavior may occur in certain allergic children. In 1922, Shannon[9] described an allergic symptom complex marked by such evidence of the "neuropathic diathesis" as restlessness, irritability, and insomnia. In 1927, Kahn[4] confirmed and enlarged on this concept. He reported not only evidence of heightened reactivity, but also a certain languidness or toxemia. Both of these workers were insistent that the symptoms described constituted a distinct syndrome which was not secondary to other allergic disorders.

In the year that have followed these pioneer observations, a considerable literature has accumulated. Since there is nothing else quite like this behavior pattern, it is not easily described and a terminology that is rather involved and disorganized has resulted. However, a consideration of these terms will reveal that they represent the endeavor of the various writers to portray a clinical picture which is dominated by two fundamental, contrasting manifestations. The first of these may be termed *allergic tension.* It is represented by evidence of hyperkinesis and hyperirritability. The second is manifested in a state of diminished activity and response known as *allergic fatigue.*

In most of the cases to be presented here, the tension-fatigue state is accompanied by little other evidence of allergic sensitization. This "pure" type of case has been selected for the purpose of emphasizing the importance of this syndrome as a clinical entity in its own right.

CASE REPORTS

Case 1.—K. B., a little girl just past two, was subject to nervousness, night crying, and listlessness. She had been breast-fed without incident, but after being weaned she seemed to have a continual "cold" and to be restless and fretful. When egg was given, the child would invariably vomit, and a rash would appear about the mouth. There was marked susceptibility to colds, and attacks of sore throat with fever occurred as often as every four or five weeks. Examination of the nasal mucosa revealed edema, pallor, and a thin discharge. The child appeared pale, and there was prominent infraorbital edema. Scratch tests revealed 2 plus reactions to Alternaria, Hormodendrum, Penicillium, and cottonseed and 1 plus reactions to house dust, cat hair, and orris root. Prompt improvement followed management of inhalant allergy, but the symptoms referable to the nervous system improved but little. A series of food eliminations was begun. The omission of milk and chocolate gave no relief. With the careful elimination of egg, the child became calm and happy and slept soundly at night. During the intervening two years, attempts to return egg to the diet have invariably been followed by restlessness, insomnia, and fatigue.

From the Allergy Clinic, University of Kansas Medical Center, Kansas City, Kansas, and the Allergy Clinic, Children's Mercy Hospital, Kansas City, Missouri. Presented before Ninth Annual Congress of the American College of Allergists, April 28, 1953.

Case 2.—G. T., a seven-year-old boy, was brought in by his grandmother because of nausea, pains about the heart, poor appetite, listlessness, difficulty getting his breath, and general nervousness. At times he would complain of "feeling hot all over," and at other times he would feel "shaky inside." He vomited easily and was subject to epistaxis, enuresis, and constipation. He frequently complained of dull aching over one eye.

His paternal grandmother was the informant. She was herself the victim of migraine, but had learned that attacks were less frequent and severe if she avoided egg, bean, peanut, and cantaloupe. The child's mother was at the home of her mother in another city. She had been there six months because she suffered so severely from migraine that she was incapacitated much of the time. There were several other persons in both families who complained of "sick headaches."

Physical findings were meager. The child was somewhat pale and listless and appeared petulant and unhappy. Routine blood counts, tuberculin test, and urine analysis were negative. The bewildering variety of complaints suggested either a psychogenic or allergic behavior disorder. The fact that the mother had left the child for a highly dubious reason made a psychogenic etiology suspect. The gastrointestinal and nervous manifestations in a child with a bilateral history of migraine favored an allergic etiology. After consultation with the family it was decided to defer any psychiatric consultation and proceed from the standpoint of allergy. Scratch tests for the common inhalants and foods were negative. A series of food eliminations was projected. Milk was the first food to be omitted from the diet. It seemed apparent within forty-eight hours that this was a fortunate choice. There was a dramatic improvement in the multitude of complaints, and the boy became relaxed, alert, and cheerful. He was well aware of his improvement himself, and spoke of how much more energy he had, and stated that he was without headache and general achiness for the first time in his memory. At the end of a week, milk was returned to his diet. The reaction was a classic migraine attack, the first the child had experienced. For the next two days he was restless, pale and irritable. He remains totally intolerant of milk, and after three years' observation it is clear that his whole multitude of seeming neurotic complaints was associated with allergy to that food.

Case 3.—When J. P. was one year old, his parents brought him in because he was constantly fussy and listless. There had been a stormy early infancy. At two weeks the child had a "blue spell," and his nose seemed constantly blocked thereafter. He cried day and night for five months, and had remained restless and unhappy ever since. His father always vomited on eating either pork or fish, and the mother and maternal grandmother suffered from migraine. The infant was put on Mullsoy. The result was prompt disappearance of excessive perspiration, blocked nose, and constipation. The irritability was greatly improved, but he still had days when "nobody could live with him." Elimination of egg gave no relief. When he was taken off cereals there was a prompt cessation of restlessness and fretfulness. This child has been under observation for four years, and during this time it has been learned that he must totally avoid milk, wheat, and corn.

Case 4.—The presenting complaints of C. N., a six-year-old girl, were tiredness, mild headaches, leg aches, vomiting, and night sweats. Her sluggishness had progressed to the point where she did not want to engage in ordinary play activities. She volunteered that her leg discomfort was a "nervous achiness." The immediate family revealed some interesting food intolerances. The child's mother affirmed that corn invariably gave her a migraine attack, and the father was known to vomit whenever he ate fresh tomatoes. Routine laboratory findings and scratch tests were negative. Food eliminations were done and corn and chocolate were at length identified as

responsible for tension, fatigue, dull headache, and nausea. This intolerance has been found to persist over an observation period of five years.

Case 5.—R. W., a four-year-old boy, had a history of frequent colds, mouth breathing, and cough. Skin tests were strongly positive for Alternaria, and hyposensitization was successful. After he had been under treatment about ten months, his mother expressed concern because of his "unusually bad disposition." She had thought it to be a result of his frequent illnesses, but now that he was doing so well with his respiratory problem she could not understand why he was so cross and antagonistic. At this time a history of severe and prolonged colic was obtained and a milk-free diet was ordered. Within a matter of days, the child seemed to undergo a complete personality change. He became bright and contented for the first time, and accepted discipline and routine in a manner that was entirely new. In the intervening eighteen months it has been found that ingestion of milk is consistantly followed by a return to his former disturbed behavior.

Case 6.—T. C., a boy, was first seen at the age of nine months because of diarrhea. There had been feeding difficulties since birth. He had always had loose stools with frequent outbreaks of frank diarrhea. There was no obvious colic, but he had always been restless and cross. Concerned as she was about his abnormal stools, the mother was much more concerned because of his unhappy disposition. When asked about excessive perspiration, she replied that he was constantly wet with sweat, especially about the head. The child was put on a Mullsoy formula and all cow's milk and dairy products were withheld. These measures were followed within two days by marked improvement. The stools became soft and formed, and the hyperhidrosis improved greatly. The child relaxed and became normal in his sleeping habits and responded for the first time to advances designed to make him smile and talk. He has remained a happy and contented baby through an observation period of two years. Attempts have been made to return milk to the diet, but these lead to a complete relapse of tension, hyperhidrosis, and diarrhea.

DISCUSSION

A review of these case histories will reveal that although there is inevitable variation from child to child, an underlying uniformity prevails that makes possible the description of a typical clinical picture of allergic tension and fatigue. The impression given is that of a child who is torn between two extremes of feeling; at one extreme, over-reactivity or tension; at the other, under-reactivity or fatigue. Most children show reactions in both fields, but for descriptive purposes it is useful to discuss them separately.

The state of tension seems to be made up of a motor component and a sensory component. Increased *motor* activity is represented in hyperkinesis, restlessness, and inability to relax. Where this reaction is dominant, the physician can see for himself the problem that confronts both parents and teacher. In the consultation room the child is constantly on the move, opening and closing doors, flitting from one book or instrument to another, interrupting conversations, and creating a general commotion.

Increased *sensory* reactivity leads to emotional instability, fretfulness, and insomnia. These children are described as "nervous" or "high-strung." Their increased reaction to the environment makes adjustment to the

stresses of childhood difficult, and they are much given to tears, pouting, and tantrums.

Fatigue, too, seems to have motor and sensory elements. Motor fatigue is represented by listlessness, sluggishness, and vague muscle aching. In these cases the child often complains of being tired, and will come in from play to rest. On the sensory side, the child is subject to torpor, and may actually appear mentally retarded. It is not uncommon for parents to remark that the child appears as if he has been "doped."

It is not within the scope of this communication to explore the techniques of diagnosis and treatment. However, it should be made very clear that before an allergic origin is considered in a behavior problem, differential diagnosis must exhaust a wide variety of psychic and somatic influences.[8] With the elimination of these, a diagnosis of allergic tension-fatigue may be considered even in the absence of other evidences of allergy. Diagnosis is confirmed by demonstrating the role of the specific allergen in the clinical manifestations of tension and fatigue. Foods are the most common offenders, and are found in approximately this order of frequency: milk, chocolate, egg, and corn.

SUMMARY

1. Clinical histories of six children are presented to illustrate the syndrome of allergic tension and fatigue.

2. Allergic tension represents a widespread exaggeration in motor activity (hyperkinesis) and a corresponding increase in sensory reactivity (hyperirritability.)

3. Allergic fatigue, in direct contrast to tension, is marked by a sensation of being tired and torpid.

4. Allergic tension-fatigue merits a place in the differential diagnosis of behavior problems of childhood.

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ANAPHYLACTOID REACTION FROM ACTH

Report of a Case

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A SURVEY of the literature reveals that allergy to ACTH is not uncommon, but only a few cases of severe immediate reaction have been reported, and in these few cases the results of investigation have not always been similar. Anderson[1] and Wilson[5] reported cases of protein shock when ACTH was given by intravenous drip, but Wilson was able to give one of these patients intramuscular injections of the hormone without complications. Driscoll[3] et al, described a case of anaphylaxis following the simultaneous injection of ACTH and novocaine, and discovered that subsequent testing gave immediate skin reactions to both drugs. He was able to desensitize his patient and thus continue ACTH therapy. Seven cases of anaphylaxis were described by Brown and Hollander.[2] Several of these patients were able to tolerate a beef gland preparation instead of the usual commercial pork preparation. They had presumably developed a specific allergy to the animal protein. In the case described by Feinberg,[4] skin tests revealed sensitivity to both pork and beef ACTH. His patient gave, as well, skin reactions to anterior and posterior pituitary extracts. The following case illustrates a more specific type of allergy, since skin reactions were obtained with both beef and pork ACTH, but only with anterior pituitary extract.

CASE REPORT

The patient is a thirty-five-year-old colored woman with a long history of allergy. She was first treated with ACTH by her physician in October, 1952, and since then has received the hormone on twelve occasions, almost all of them during the 1953 ragweed season. Recently she suffered a severe attack of asthma, and once again ACTH was administered. She left the physician's office to return home. One hour later, she suddenly felt very hot, developed generalized giant hives with nausea and diarrhea. She felt weak and had to lie down. Her face and lips swelled, her voice became so husky that she could not speak, and she had difficulty with breathing. She took two tablets of Tedral® and called the doctor, but before he arrived she began to feel better, and the reaction gradually subsided. (It is interesting to speculate how much the ACTH was responsible for curing its own reaction!)

Since much of her reaction was gastrointestinal she attributed it to a harmless bottle of cough syrup, but readily agreed to skin testing and was much amused when both scratch and intradermal tests remained negative after thirty minutes. However, she was honest enough to report next day that two hours later, she had intense itching and found large wheals in both sites. Accordingly she was asked to report back two hours after the next session and the skin tests were repeated. To

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Dr. Swift is an Associate Fellow of the American College of Allergists.

our mutual surprise, immediate whealing with pseudopodia took place. Throughout her treatment the ACTH preparation used was the aqueous solution made by the National Drug Company of Philadelphia.

INVESTIGATION

The next week, the following skin tests were carried out using the intradermal technique with the reactions indicated:

1.	ACTH National (pork) aqueous	3+
2.	ACTH National (pork) gel	1+
3.	ACTH. Armour (beef) aqueous	4+
4.	Pork extract	0
5.	Beef extract	0
6.	Posterior pituitary extract	pressor reaction only
7.	Pitocin	0
8.	Anterior pituitary extract	3+
9.	Control	0

It will be seen that the positive reactions were limited to anterior pituitary substances. Unfortunately one is not able to be any more specific than this, since no other anterior pituitary hormone is available.

Passive transfer was carried out in two subjects, with identical results in both cases. Positive reactions in the prepared sites were obtained with ACTH pork, both aqueous and gel, ACTH beef and with anterior pituitary extract. Control tests were all negative except in the case of the beef ACTH which produced false positive reactions to some extent in all the dilutions used.

SUMMARY

A case of violent allergic reaction to ACTH is described. Skin testing demonstrated reactions to both beef and pork ACTH, a lesser reaction to the more highly purified gel preparation, and a reaction to anterior pituitary extract. Passive transfer was carried out and the prepared sites showed reactions identical with those of the patient.

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EXPERIENCES WITH PIROMEN IN THE TREATMENT OF ALLERGIC DISORDERS

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THE recognition and treatment of allergy in the past thirty years has shown marked progress. More and more conditions of previously unknown etiology are now being classified as allergic in origin.

A few of the milestones on the road to a better understanding of the allergic state may bear repeating: (1) the development of potent extracts for testing and treatment, (2) the reproduction of symptoms in cases of possible food allergy by test feeding after elimination of the suspected food from the diet for a few days, rather than reliance on skin tests, (3) the use of elimination diets in the diagnosis of food allergy, (4) the pulse-diet technique of Coca, (5) the stress concept of Hans Selye, (6) the recognition of psychosomatic factors, (7) the development of adrenocorticotropic hormone (ACTH) and the corticosteroids, (8) the discovery of the antihistaminics, (9) and finally the awakening interest in nutritional adequacy as a prerequisite for normal body chemistry.

In spite of these advances every physician encounters refractory cases that respond unsatisfactorily to every therapeutic effort. A nontoxic, nonspecific substance capable of mobilizing body defenses against allergic attack has long been sought. Piromen®* showed promise in this respect and its clinical application forms the basis of this preliminary report.

PHARMACOLOGY AND OTHER PROPERTIES

Piromen is a sterile, colloidal solution containing a complex polysaccharide obtained from a relatively nonpathogenic strain of Pseudomonas aeruginosa. Intensive studies from pharmacologic and clinical aspects have shown it to be relatively nontoxic and nonanaphylactogenic.[7,8]

Some investigators have found evidence in both animals and humans that injections of Piromen produce a leukopenia followed in a few hours by a neutrophilic leukocytosis. This suggests stimulation of the pituitary-adrenal axis.

The leukocytic response to ACTH in dogs disappears following adrenalectomy, whereas that to pyrogens remains.[12] In cats, however, bilateral adrenalectomy abolishes the characteristic leukocytic response to both these compounds. The variable results may be due to technical difficulties or a species difference.[6]

Windle, *et al,* working with rabbits, have found evidence of adrenal

*Piromen was courteously supplied by Robert P. Herwick, M.D., Medical Director of Travenol Laboratories, Inc. (Subsidiary of Baxter Laboratories, Inc.)

cortical hypertrophy together with hyperactivity of the bone marrow, lymph glands and spleen following repeated doses of Piromen.[13,14] In other words, activation of the reticuloendothelial system.

The action of Piromen on connective tissue suggests the inhibition of fibroblastic proliferation and the enhancement of vascularization. Thus glial scar tissue is reduced and the growth of neurons through transected, feline spinal cords facilitated.[1,11,15,16]

The work of Green[3] is of dramatic interest. In a study of severely burned rats, this observer found that a single optimal dose of Piromen given within six hours after a burn, was as effective as multiple doses and resulted in an 87 per cent survival rate as compared to 100 per cent mortality in the control group. Sub-lethal burns healed more rapidly and with better epithelization than the controls. Experimental evidence thus supports the concept of an endocrine, reticuloendothelial and peripheral action.

Encouraging clinical reports in the treatment of perennial allergic conditions, poliomyelitis, neurodermatitis and depressed emotional states have recently appeared in the literature.[2,4,5,9,10,17,18]

METHODS

The present contribution is entirely clinical and without controls, except that most cases were of a chronic nature and had responded poorly to previous treatment. Piromen was used alone in thirty-nine cases and added to prior therapy in thirty-one. Nutritional support as indicated was basic in all.

Under these circumstances such potent therapeutic agents as ACTH and Cortisone would have produced a high percentage of at least temporary response. Such was not the case in this series and yet some very interesting results were observed.

Seventy patients were treated for a long enough period to be included in this report. Duration of treatment varied from three days to twenty-two months. With the exception of poison oak dermatitis, the minimum period was three weeks. Improvement, if it were going to occur, almost always appeared before the sixth injection.

Ages ranged from a tender two years to a mellow seventy-two. Of eighteen patients under the age of fifteen years, the number responding favorably to Piromen was fifty per cent greater than the average for the whole group. This is not surprising, for youth is resilient.

Two-thirds of the patients were females and one-third males. Allergic conditions treated included the following: asthma 24, dermatitis venenata 10, allergic rhinitis 9, neurodermatitis 6, hay fever 4, chronic urticaria 2 and miscellaneous conditions such as penicillin reaction, Hunner's ulcer, herpes labialis, neuritis, acute bursitis, and migraine 15.

Piromen injections were given intravenously in half of the cases and intramuscularly or subcutaneously in the remainder. Treatment was usually

initiated with 1 gamma and increased by 1 gamma every two or three days until improvement or constitutional reaction occurred. The dose was then stabilized or reduced 25 to 40 per cent in the case of reactions and held at that level. Relief of symptoms was an indication for repeating the same dose at intervals of one to three weeks as necessary to maintain remission.

Considerable individual variation in tolerance was soon apparent. The average dose by both routes of administration was between 0.5 and 10 gamma, with most cases receiving 5 gamma or less. The smaller doses may be more desirable and the subcutaneous route preferable.

While some cases were treated no oftener than once weekly, dermatitis venenata due to poison oak seemed to warrant daily injections.

One patient tolerated 50 gamma intravenously without reaction or improvement. An asthmatic child of eight, under treatment with ACTH for intractable asthma, was given large intravenous doses in hopes of producing a remission. In spite of 30 gamma, followed by 60 gamma two hours later, a temperature of only 100.6 was achieved. The antipyretic effect of ACTH has been noted before. No benefit was obtained. In contrast, symptoms have been provoked by as little as 0.5 gamma intravenously and subcutaneously. Children and elderly people must be treated cautiously.

Constitutional reactions consisted of malaise, generalized aching, chilly sensations (one tooth-chattering chill), headache and fatigue lasting from one to twelve hours. No sequellae were observed. Following intravenous therapy the reactions occurred within two hours, but were delayed as a result of the subcutaneous route. A few asthmatics developed increased wheezing, but no anaphylactoid reactions were noted. Others, however, have reported fairly severe asthmatic flareups. This again suggests the subcutaneous route as being more desirable.

In a few cases repeated subthreshold doses eventually resulted in a reaction requiring reduction in future doses. In others, increasing tolerance necessitated a gradual increase in dosage to maintain improvement. A few relapses following original improvement may be based on the development of a refractory state. There was no apparent correlation between the elicitation of a reaction and the results obtained.

RESULTS

Slightly more than half the cases obtained definite amelioration of symptoms. In about one fifth of the total, relief was very satisfactory. Seven individuals with severe, wide-spread skin lesions due to poison oak were comfortable after two or three daily injections of 5 to 10 gamma and the lesions had begun to regress. If these cases are removed from this series, only one half of the remainder could be considered improved, but of this thirty-five, fourteen were in the category of markedly improved. The poison oak group was classified as moderately helped. Perhaps this is too conservative.

CASE REPORTS

Case 1.—V. S., a seventy-one-year-old male, complained of progressive wheezing, dyspnea and weakness of twelve years' duration. He was getting some relief from aminophylline by mouth and Adrenalin by inhalation. Skin tests were negative. History included a twenty-five-year exposure to dust in a gold and silver mine. Roentgenograms showed pneumoconiosis with marked fibrosis. There was no eosinophilia. Improvement was continuous after three weekly intramuscular injections which were thereafter given twice weekly. Maintenance dose is 8 gamma once a week. There has been a marked gain in strength and eight pounds in weight. Wheezing is much improved and medication is needed only occasionally.

Case 2.—H. Q., a young man of fifteen, has had severe allergic rhinitis and asthma for twelve years. The onset followed pneumonia. Skin tests were positive to spring, summer and fall pollens and to house dust. Milk was an offender. Elimination diets and hyposensitization were ineffective. He has received 1 to 2 gamma of Piromen intravenously twice weekly for five months with repeated mild constitutional reactions. Although asthmatic attacks seem less frequent and less severe, there has been no significant improvement.

Case 3.—S. R., a girl of seventeen with a history of hay fever, recurrent urticaria and asthma for eleven years, has received intravenous Piromen in doses of 5 to 10 gamma once weekly for seven months. Sensitivities include house dust, tree and weed pollens. Improvement was noted after the second injection and has continued to date. Symptoms are now very mild and medication seldom needed. She has been carried through her pollen seasons without flareups.

Case 4.—Mrs. R. D., a housewife, aged sixty-one, gave a long history of asthma, paroxysmal tachycardia, hypertension, colitis and fatigue. By means of Coca's pulse technique, numerous foods and house dust were found responsible and improvement was marked. Fatigue and mild symptoms remained as a result of encountering minor food and inhalant allergens. A gratifying sense of well being appeared after the first hypodermic of 1 gamma of Piromen, which was substituted for house dust she was receiving in the same manner. Injections were given twice weekly at first with a top dose of 1.5 gamma. She now "feels like a new woman" and can tolerate minor food allergens without symptoms. Major food offenders must be avoided, however. A three week interval was too long and the injections are now given once every two weeks.

Case 5.—E. McL., a man of fifty-six, had suffered from recurrent nasal polypi, profuse, thick nasal discharge and severe asthma for four years. No etiologic factors could be incriminated. Onset followed pneumonia. Antibiotics were of no help in preventing repeated status asthmaticus. Eosinophils in the peripheral blood averaged 20 per cent. Stools were negative for parasites. While taking cortisone, with excellent control of asthma and nasal complaints, he was given 4 gamma of Piromen intravenously three times weekly for a period of three weeks. During this time cortisone was gradually withdrawn, but his asthma returned in full force. When last heard of five months later he was living in another city and still taking cortisone.

DISCUSSION

It was interesting to note that in those cases showing improvement there was no obvious change in circulating eosinophiles.

With the exception of the poison oak cases, all of which responded, im-

provement in other categories was about fifty per cent. If the major allergic complaint was relieved, other manifestations improved concomitantly.

A small series of cases such as this is not suitable for statistical analysis. Clinical evaluation is difficult because of many extraneous factors that do not lend themselves to control. Emotional and other forms of stress may vitiate the effects of therapy that might otherwise prove successful. Conversely, relief of tension may induce improvement and the result be attributed to whatever medication is being used at the time.

It is possible that relapses observed in a few patients responding favorably at first may be controlled by shifting to a pyrogen of different origin. It is also possible that a better understanding of optimum dosage may improve results.

Obviously, Piromen is not the long-sought panacea for the treatment of allergic disorders. It should not therefore be relied upon as a routine form of therapy for these conditions. However, the impressive response of a small number of patients suggests that it will find a place in the treatment of selected cases, particularly when major allergens have been sought for, discovered and controlled insofar as that is possible.

The results obtained in the treatment of dermatitis venenata due to poison oak are particularly encouraging. Further evaluation is needed.

SUMMARY

Seventy cases with a variety of refractory allergic disorders were treated with injections of Piromen (a standardized extract of Pseudomonas aeruginosa containing a complex polysaccharide). A scant majority responded with significant improvement. Seven cases of poison oak dermatitis showed a uniformly good response. Piromen is not recommended as a substitute for routine allergic management, but is of value in selected cases.

ADDENDUM

Since this paper was written, twenty-six additional cases of poison oak dermatitis have been treated with Piromen, utilizing a daily *hypodermic* dose of 2 gamma. Most of these individuals had received prior therapy and the disorder had been present for one or more weeks without improvement. Two of these required ACTH on the fourth day of treatment because of poor response; the remainder were comfortable by this time. From two to eight injections were needed for clinical cure. Most patients responded to three or four.

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WOMEN'S AUXILIARY TO THE AMERICAN COLLEGE OF ALLERGISTS

On Thursday, April 8, 1954, there was a meeting of the wives of the members of the College, at Miami Beach, Florida, for the purpose of inaugurating a Women's Auxiliary to the College. The meeting was well attended and there was much enthusiasm over the advantages of such an auxiliary. Articles of incorporation were drawn up by the Counsel for the College and these will be published in a future issue of the ANNALS. Its aims and purposes, as set forth therein, represent the highest ideals and efforts for the wives of the members to aid the College.

The first officers were elected at this meeting, as follows: President, Mrs. Morris Kaplan, Chicago; President-elect, Mrs. Ethan Allan Brown, Boston; Vice President, Mrs. Fred W. Wittich, Minneapolis; Secretary, Mrs. J. Warrick Thomas, Richmond, Virginia; and Treasurer, Mrs. Boen Swinny, San Antonio, Texas.

DRAMAMINE (INJECTABLE) IN MIGRAINE

Preliminary Report

MAURICE VAISBERG, M.D.

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IN DECEMBER, 1952, during the course of some investigational work with Dramamine Injectable, hereafter known as D1, it was thought that the intense nausea and vomiting of migraine might be helped by injection of D1. A series of 100 attacks of migraine in fifty patients was treated with D1 with amazingly consistent and dramatically rapid gratifying results. In each instance there was complete subsidence not only of the nausea but total relief of the pain within a matter of four minutes when the drug was given intravenously* and within a quarter of an hour when administered intramuscularly. The dose varied from 50-100 mg. In some cases there followed a gratifying drowsiness and sleep which could readily be terminated by oral amphetamine, thus enabling the patient to resume routine daily activities with renewed vigor and zest. In each instance the desire and need of the patient was followed in this regard and either sleep or wakefulness restored almost at will.

Each of the fifty patients had had a definite history of migraine and each had the psychosomatic background and environmental trigger mechanism for precipitation of an attack. At the time of administration of D1 the individual attack had been well established for a matter of from two to six or more hours. Medications which had given relief previously included pyramidon, DHE 45, codeine and, in one instance, dilaudid with intravenous luminal.

There have been some reports of excellent to poor (generally equivocal) results with oral dramamine, but one can readily understand the lack of uniformly good results in a well-established case of migraine with its attendant nausea and resultant impaired absorption.

In no instance was there a therapeutic failure after injection of D1. In a single case complete relief was obtained for only two hours and it required another injection of 2 c.c. to produce lasting (over 48 hours) relief.

From personal communication with several physicians, it was ascertained that they all achieved uniform success in completely relieving the migraine symptoms rapidly for prolonged periods of time by the injection of D1.

*For intravenous use each c.c. of Dramamine Injectable must be diluted with at least 9 c.c. of normal saline previous to injection.

Note: The Dramamine Injectable was supplied by the kindness and courtesy of Searle and Co., whose medical staff was extremely co-operative in every phase of this work.

There were no undesirable side effects. An occasional after-effect was an indurated area at the site of injection due to the shallow deposition of material into the subcutaneous tissues rather than to intramuscular placement.

SUMMARY

Dramamine Injectable, given either intramuscularly or intravenously is a potent, non-toxic, well-tolerated, non-habit forming, inexpensive and readily available medicament for the treatment and immediate prolonged relief of migraine, no matter how severe the attack may be, and no matter how long its previous duration.

7744 Bryon Avenue

CONTRIBUTIONS FOR ENTERTAINMENT AND INSTRUCTIONAL COURSE SCHOLARSHIPS

The officers of the College express their sincere gratitude for the generous contributions from the firms listed below, which in large measure accounted for the success of the Decennial Congress in Miami Beach:

Baxter Laboratories, Inc. ..... Morton Grove, Illinois
The Borden Company ..... New York, New York
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Sandoz Pharmaceuticals ..... New York, New York
Schering Corporation ..... Bloomfield, New Jersey

THE USE OF CHLOR-TRIMETON IN THE PREVENTION OF BLOOD TRANSFUSION REACTIONS

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and
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THE PREVENTION of blood transfusion reactions has long appealed to a number of investigators. Through their work many advances in the technique of transfusing blood have been made in the past twenty years. With this in mind the addition of an antihistamine to the blood apparently occurred to quite a few workers about the same time. Previous to this, however, transfusion reactions of all kinds, but mainly the allergic type, had been treated frequently with antihistaminic drugs orally and by intramuscular or intravenous injection.

Baratta[2] reported on the use of an oral antihistamine (Chlor-Trimeton Maleate®) given periodically for twenty-four hours preceding transfusion. He treated reactions by intramuscular injection of the same drug. In emergency cases and in sensitive patients the drug was added to the blood shortly before transfusion.

Alfonsi[1] added 200 mg. of Antistine® per 500 cc of blood transfused in 350 patients with another 350 used as controls. He observed fifty-three chill-fever reactions in the controls and only fourteen in those receiving the antihistamine. The controls produced fifteen allergic reactions, twelve urticarial and three eruptions, while there were none in those receiving the antihistamine. He felt that the reactions which occurred in spite of the antihistamine were due to pyrogens of a non-protein or carbohydrate nature which therefore did not have antigenic properties.

Ferris, Alpert and Coakley[4] added 25 mg of Pyribenzamine® to each of 607 pints of blood while 742 were used as controls. Where the antihistamine was used there were two reactions, one allergic and one hemolytic, a percentage of 0.32. Without the antihistamine there were twenty allergic and thirty-two pyrogenic reactions, a percentage of 7.1.

Bernstein and Klotz[3] reported on the therapeutic efficiency of Chlor-Trimeton Maleate® given intravenously and this was followed by several studies of others on its use in blood transfusion.

Frankel and Weidner[5] reduced the reaction rate which in 308 controls was 3.5 per cent to 0.3 per cent in 284 transfusions by adding 10 or 20 mg of Chlor-Trimeton to the blood.

Offenkrantz, Margolin and Jackson[6] first showed that there was no significant difference in blood stored with or without Chlor-Trimeton

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Read by title at the Decennial Graduate Instructional Course, The American College of Allergists, Miami Beach, Florida, April 5-7, 1954.

added. Their control series of 350 cases manifested twenty-two reactions or 6.3 per cent. Where 10 mg of Chlor-Trimeton were added to the blood in 300 transfusions there were two reactions or 0.6 per cent.

TABLE I. BLOOD TRANSFUSION REACTIONS WITH AND WITHOUT CHLOR-TRIMETON

Number of Transfusions	Amount of Chlortrimeton Added	Allergic Reactions	Pyrogenic Reactions
394	5 mg.	1 (.25%)	1 (.25%)
467	None (Controls)	2 (.43%)	1 (.21%)
987	10 mg.	0	2 (.21%)
995	None (Controls)	10*(1%)	8*(.80%)

*Note—One patient had both types of reaction.
The incidence of allergic reactions in all controls .82%
The incidence of pyrogenic reactions in all controls .62%

PRESENT STUDY

The series here reported was started in July, 1952, adding but 5 mg of Chlor-Trimeton* to each unit of blood. After four months the amount of the antihistamine was increased to 10 mg per unit of blood. In 394 transfusions where 5 mg were used per unit of blood, there was one urticarial and one pyrogenic reaction. In the 467 controls there were two urticarial and one pyrogenic reactions. The antihistamine was added to the blood given patients with even admission numbers and those with odd admission numbers served as controls. The appearance of even one urticarial reaction, where the antihistamine was added led to the conclusion that a higher dose was necessary. So throughout the next twelve months 10 mg of Chlor-Trimeton were added to each unit of blood used. The antihistaminic drug was in a separate vial or ampule attached to the bottle containing the blood and the doctor who started the transfusion put the required amount into the flask and then gently agitated the blood to produce adequate mixing. The results of all transfusions were reported individually by the doctors who administered them.

In the year-long series with 10 mg of Chlor-Trimeton added, there were two pyrogenic reactions in 987 transfusions or 0.21 per cent. One of these is highly questionable as the patient had 1200 cc of urine removed by catheter shortly before the blood was given. The control series of 995 transfusions produced seventeen reactions which consisted of nine urticarial, seven pyrogenic and one having both types of reaction, a percentage of 1.71 (Table I).

DISCUSSION

In agreement with the previous workers, we are convinced that the addition of sufficient Chlor-Trimeton to the blood in transfusions will eliminate allergic or urticarial reactions and markedly reduce pyrogenic reac-

*Chlor-Trimeton furnished through the courtesy of Schering Corporation, Bloomfield, New Jersey.

tions. For the figures to have real significance, it is felt that a large series is necessary and therefore the year-long study.

Offenkrantz inoculated whole blood with 20 mg of Chlor-Trimeton per unit and compared the blood with controls drawn at the same time. After 1, 3, 5, 7, 8, 11, 13, 15, 18, 20, 22 and 26 days there was no increase in hemolysis or any other observable difference. Nevertheless, we added the antihistamine immediately before transfusion to be absolutely sure there would be no change in either the blood or the drug.

No side reactions to the Chlor-Trimeton have been noted but as the most frequent one would have been drowsiness and these were all very sick patients no definite conclusions can be drawn.

Despite the contention by some authorities that the use of any agent which might mask hemolytic reactions is contraindicated, it is our considered opinion that in no case will any amount of antihistaminic drug influence this type of reaction.

SUMMARY AND CONCLUSIONS

1. In 987 transfusions where 10 mg of Chlor-Trimeton was added to each unit of blood there were no allergic reactions and only two pyrogenic reactions, an incidence of 0.21 per cent. The control series of 995 transfusions produced seventeen reactions, an incidence of 1.71 per cent.

2. Allergic reactions are eliminated and pyrogenic reactions markedly reduced when 10 mg of Chlor-Trimeton are added to each unit of blood prior to transfusion.

ACKNOWLEDGMENT

It is the desire of the authors to express their appreciation to Freeland G. White, A.B., for his invaluable assistance in this study.

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576 Daytona Parkway

CLINICAL EXPERIENCE WITH THE USE OF BIOMYDRIN® ON PATIENTS WITH RESPIRATORY ALLERGIES

Preliminary Report

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PREVIOUS reports[1,2] on the topical application of Biomydrin® have been made by otolaryngologists in the Chicago area. This environment is mentioned because the climatic factors conducive to respiratory infections are somewhat comparable to those in Minnesota. Many respiratory allergies in the latter region are complicated by acute or subacute infections of both the upper and lower respiratory tracts.

A clinical evaluation of various decongestive nose drops or sprays in persistent cases of upper respiratory infection complicating allergies is facilitated by comparing results of their use throughout the years.

Competent bacteriological studies of the flora of nasal and paranasal infections have been reported. Hemolytic *Staphylococcus aureus,* nonhemolytic and hemolytic streptococci are the predominating organisms. More recently critical observations of the composition and effect of nasal solutions on the mucous membranes would indicate a combination of one possessing vasoconstrictive, antibiotic, and antihistaminic properties giving favorable results without untoward effects would warrant a clinical trial on allergic patients with and without demonstrable infection. Biomydrin® was selected because previous favorable results with its use were reported.[1,2] It consists of a combination of two antibiotics, neomycin and gramicidin, supported by the antibacterial activity of thonzonium bromide; the antihistamine thonzylamine (Neohetramine®) and the vasoconstrictor, phenylephrine hydrochloride.

The antibiotics in the solution are stable, possess a wide spectrum of effective activity throughout a broad range of pH, and are not affected by body fluids. Their clinical use has shown that they do not lead to acquired sensitization or the induction of bacterial resistance after local application. They are particularly effective by topical use.[4,6] They are not used parenterally, which greatly diminishes the chance for possible sensitization. Both antibiotics are bactericidal so that the chance for development of bacterial resistance is lessened or slowed. *In vitro* tests with a concentration of 5 ug/ml gramicidin inhibited strains of hemolytic streptococci, pneumococci and staphylococci, and this strength is used in the combination spray. Neomycin, although active against a wide variety of Gram-positive bacteria, was selected particularly for its action against many Gram-negative bacteria such as *Hemophilus influenzae.* This antibiotic is derived from a

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From the private allergy clinic of F. W. Wittich, M.D., President of the International Association of Allergology.

Biomydrin kindly supplied by The Nepera Chemical Co., Inc., Yonkers, N. Y.

strain of *Streptomyces fradiae* and the preparation contains a concentration of 100 ug/ml.

Thonzylamine hydrochloride (Neohetramine®) in a one per cent solution is the antihistamine used in the preparation. Criep and Aaron[3] reported prompt symptomatic relief by its use in allergic rhinitis. The preparation contains phenylephrine hydrochloride in a concentrate of 0.25 per cent as the vasoconstrictor or decongestant. It has been shown from wide use that it is a powerful safe vasoconstrictor, with minimal rebound effects and relatively few cardiac or central stimulating effects when used topically. Thonzonium bromide with a low surface tension and in a concentration of 0.05 per cent is a rapidly spreading surface acting agent thus producing a prolonged action. It is also a potent bactericide which may enhance the activity of the two antibiotics.

The antihistamine (Neohetramine®) is well known to allergists as effective, possessing a low degree of toxicity and few side reactions. The addition of a vasoconstrictor[7] known to have a rapid and lasting effect, with virtual freedom from side effects, would indicate that such a constructed solution warrants its use in allergic patients, particularly when the allergy is complicated by a superimposed infection. Any topical isotonic and appropriately buffered aqueous preparation which would favor proper nasal ventilation for long periods without irritation or inhibiting ciliary activity warrants its use clinically on allergic patients.

This report describes results of the topical use of a Biomydrin spray on a group of private patients with upper and lower respiratory allergies as they presented themselves and where it was thought a selected nasal solution may be effective. The majority of these patients were receiving the usual anti-allergic measures of elimination or avoidance, hyposensitization and adjunct drug therapy. When the nasal spray was prescribed other drug medication was withdrawn with the exception of a few cases of severe asthma and/or seasonal nasal allergy. In these latter cases any increased beneficial effects of the spray were carefully noted.

The selected patients were furnished with a "squeeze bottle" atomizer containing the nasal solution and instructed to hold the head in a normal upright position, with the atomizer tip held to the nares, and apply a quick, firm pressure to deliver a fine spray mist into the nasal passage, followed by sniffing. Parents were instructed to give children one or two sprays or more, depending upon the degree of obstruction, during each application. The length of treatment extended anywhere from three weeks to as long as was necessary to obtain results. Patients were instructed to report weekly in person or by indirect communication. Thus judgment of the results was based both upon direct observation and the opinion of the patient.

Cytologic studies were made of nasal smears on all patients before and following treatment. These consisted of enumeration of eosinophils by the Hansel[5] technique and Gram stain for a notation of the predominating

Gram-positive and Gram-negative bacteria. Estimation of clinical results was recorded as excellent, good, fair and poor.

It will be noted in the accompanying table that the percentage of eosinophils represent an average before and after treatment. Like the blood eosinophilia, the eosinophils of the nasal secretions vary at different periods depending upon the amount of superimposed infection, as well as a fluctuation in any given patient at a particular period of allergic activity. If there was any doubt about a superimposed infection, cultural studies were made.

RESULTS

Of eight uncomplicated seasonal hay fever cases, seven obtained excellent, and one good relief during treatment with Biomydrin spray. This small number out of a series of thirty-five patients treated indicates the comparative incidence of uncomplicated seasonal hay fever cases in the Minnesota area as compared with those who have a perennial respiratory and/or infectious element. This confirms previous observations through the years.

Of twelve patients with respiratory allergy with an infectious nasal complication, two revealed excellent, six good, and four poor results.

Of fourteen patients with perennial respiratory symptoms with no definite evidence of chronic infection, seven obtained excellent, six good, and one fair relief. One patient with a strong psychogenic component obtained no relief.

In accord with previous observations,[1,2] such pathogens as were found in nasal smears before treatment were eliminated from post-treatment smears of many of the Biomydrin-treated patients.

Sufficient controls were made of hay fever patients who had received no nasal medication or a placebo during the season to reveal that these latter patients were definitely less comfortable and had less control of their nasal symptoms than did patients treated with the spray. This applied also to the perennial nasal allergic patients.

SUMMARY

Thirty-five patients with respiratory allergies, either seasonal, perennial, or with a superimposed infection were treated daily with the spray through a period of time. The over-all picture of the results following its use showed a comparatively greater margin of clinical improvement than in the control group. Thirty of the thirty-five patients had good to excellent results. Five had a poor result—an over-all average of 85.7 per cent improvement in this group of cases.

Patients with uncomplicated nasal allergies, seasonal or non-seasonal, obtained good results during its use. The patients with a definite superimposed infection obtained better results when the infection was acute than when the infection was chronic. In these patients with acute nasal

TABLE I. EVALUATION OF THE USE OF BIOMYDRIN IN ALLERGIC PATIENTS WITH RESPIRATORY ALLERGY

Case No.	Age	Clinical Diagnosis	Cytology		Estimate of Clinical Result
			Before (Average)	Following Spray	
1	45 yrs.	Fall Type Hay Fever	50% Eosinophils	Little change	Excellent during season only
2	28 yrs.	Spring, Fall Hay Fever	80% Eosinophils	Little change	Excellent during season only
3	38 yrs.	Perennial Allergic Rhinitis, with Seasonal Exacerbations and Superimposed Infection	10% Eosinophils Gram-positive Strep. & Staph.	No pathogens	Excellent during course as well as during infectious colds.
4	9 yrs.	Per. Allergic Rhinitis Per. Asthma, Hay Fever (Fall). Frequent Upper Respiratory Infections	100% Esoinophils Gram-positive Staph. & Strep. during colds. Av. 20% Eosin, during colds.	No pathogens	Good
5	48 yrs.	Per. Allergic Bronchitis Per. Allergic Rhinitis Seasonal Hay Fever	50% Eosinohpils. Few Gram-positive Staph.	No pathogens	Good
6	11 yrs.	Per. Allergic Rhinitis Per. Asthma (Infectious element)	3% Eosinophils. Numerous Gram-positive Staph.	No pathogens	Good
7	28 yrs.	Per. Allergic Rhinitis with infectious element	20% Eosinophils. Few Gram-positive Staph. & Strep.	No pathogens	Good
8	15 yrs.	Per. Allergic Rhinitis	3% Eosinophils. Few Gram-positive organisms	Few pathogens	Good
9	9 yrs.	Per. Allergic Rhinitis	50% Eosinophils. Few Gram-positive organisms	No pathogens	Excellent
10	60 yrs.	Seasonal Hay Fever Chronic Infectious Sinusitis	80% Eosinophils. Few Gram-poistive Staph.	No pathogens	Excellent during use
11	34 yrs.	Seasonal Hay Fever (Fall)	50% Eosinophils. No Gram-positive organisms.	No pathogens	Excellent during season
12	63 yrs.	Per. Bronchial Asthma Per. Allergic Rhinitis Chronic Infectious Sinusitis (Polypectomy)	10% Eosinophils. Numerous Gram-positive and Gram-negative organisms		Poor
13	16 yrs.	Per. Allergic Rhinitis (Urticaria)	5% Eosinophils. Few Gram-positive Staph.		Good during use
14	28 yrs.	Per. Asthma Per. Allergic Rhinitis Seasonal Hay Fever	3% Eosinophils (out of season) Few bacteria	No bacteria	Excellent
15	65 yrs.	Per. Allergic Asthma & Rhinitis (marked nasal symptoms, infections)	9% Eosinophils. Numerous Gram-positive Strep. & Staph.	Same	Poor
16	60 yrs.	Per. Allergic Rhinitis	15% Eosinophils. No pathogens	Same	Excellent
17	24 yrs.	Per. Allergic Rhinitis Superimposed Infection	11% Eosinophils. Numerous pathogens	Same	Poor
18	13 yrs.	Bronchial Asthma Per. Allergic Rhinitis	15% Eosinophils. Few bacteria	Same	Fair after two weeks medication
19	33 yrs.	Per. Allergic Rhinitis Per. Allergic Asthma Seasonal Hay Fever (Fall)	50% Eosinophils. Few pathogens	No pathogens	Good. More than temporary relief.
20	53 yrs.	Per. Allergic Rhinitis Per. Bronchial Asthma Superimposed Chronic Sinus Infection	50% Eosinophils. Gram-positive Strep.	No pathogens	Nasal relief good during use—no asthma since.
21	23 yrs.	Per. Allergic Rhinitis Per. Bronchial Asthma	100% Eosinophils. Few gram-positive bacteria	No pathogens	Good during use
22	38 yrs.	Per. Allergic Rhinitis with Seasonal Hay Fever Chronic Infectious Sinusitis	100% Eosinophils (during season) Few gram-positive Strep.	Same	Poor
23	10 yrs.	Seasonal Hay Fever (Fall)	100% Eosinophils No pathogens	Same	Excellent during season
24	18 yrs.	Seasonal Hay Fever (Fall)	75% Eosinophils No pathogens	Same	Excellent during season
25	34 yrs.	Seasonal Hay Fever (Spring & Fall Type)	60% Eosinophils No pathogens	Same	Good during season
26	58 yrs.	Seasonal Hay Fever (Fall)	70% Eosinophils No pathogens	Same	Excellent during season
27	22 yrs.	Seasonal Hay Fever (Grass and ragweed)	35% Eosinophils No pathogens	Same	Excellent during season

TABLE I. EVALUATION OF THE USE OF BIOMYDRIN IN ALLERGIC PATIENTS WITH RESPIRATORY ALLERGY—CONTINUED

Case No.	Age	Clinical Diagnosis	Cytology		Estimate of Clinical Result
			Before (Average)	Following Spray	
28	20 yrs.	Per. Allergic Rhinitis Seasonal Hay Fever (Fall) Infectious element	50% Eosinophils Num. Gram-positive Staph.	No pathogens	Good during season Fair out of season
29	5½yrs.	Per. Allergic Rhinitis Hyperplastic Sinusitis (Infectional element)	10% Eosinophils Few pathogens	No pathogens	Good during use
30	36 yrs.	Per. Allergic Rhinitis Seasonal Hay Fever (Fall)	50% Eosinophils No pathogens	Same	Excellent
31	47 yrs.	Per. Allergic Rhinitis Seasonal Hay Fever (Fall)	100% Eosinophils No pathogens	Same	Excellent during hay fever season—fair following
32	32 yrs.	Per. Bronchial Asthma Seasonal Allergic Rhinitis—strong psychogenic component	15% Eosinophils Few pathogens	No pathogens	Poor
33	52 yrs.	Per. Allergic Rhinitis	25% Eosinophils No pathogens	Same	Good during use
34	46 yrs.	Recurrent Bronchial Asthma Per. Allergic Rhinitis. Seasonal Hay Fever (Fall)	40% Eosinophils. Few Gram-positive Staph.	No pathogens	Excellent during hay fever season—fair out of season
35	40 yrs.	Recurrent Bronchial Asthma. Seasonal Hay Fever (Fall)	10% Eosinophils (out of season) No pathogens	Same	Excellent—no return of symptoms during past year

infections, most of the infections were aborted and there was no subsequent invasion of the lower respiratory tract.

In the chronic superimposed nasal infection which aggravated the asthma due to a bacterial allergy or infection, there was a notable improvement of the asthma symptoms in some if the spray was used as infrequently as once or twice daily.

During this study numerous occassions arose where patients with no apparent allergies were treated at the onset of upper respiratory infections and such treatment was found successful in aborting colds. Colds in patients treated with this nasal medication were usually of shorter duration and less severe than in an untreated group.

Although observations were made on a comparatively small number of patients with respiratory allergies, the therapeutic results with Biomydrin nasal spray as described warrants its further use.

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401 LaSalle Bldg.

THE ALLERGY LIFE LINE

M. J. GUTMANN, M.D.
Jerusalem, Israel

IT is of great practical advantage to the physician to get a swift and intelligible survey of the sequence of allergic events in his patient's life. With this purpose in mind, I have drawn a simple graphic representation, which I call the Allergy Life Line (A.L.L.) (Chart I).

Two small squares are provided for every age (columns I and III), in which the particular allergic diseases are marked down (according to the index at the left side of the table). In between these two columns, there is a vacant one (II) denoted "W," meaning the "working line" which shows the patient's working capacity at all times. When referring to children, it means that they can perform their usual tasks like going to school or to the kindergarten. If the usual occupation is suspended by the disease, this column is filled in black.

The last column (IV) serves for pointing out particular conditions, such as menstruation, pregnancy, desensibilization, special treatments as with ACTH, cortisone, et cetera.

Finally, there is a symbol for "protective care," which designates that the patient is working only while under a certain protection such as a special climate, for example; whereas, if he were in another climate, he would immediately suffer from asthmatic attacks again. Similarly, suspension of protective care in a patient who is well only while under a strictly kept dietetic regime is at once conducive to reappearance of morbid manifestations. We believe this distinction to be important in that it keeps us from entertaining erroneous impressions of genuine cure.

I should now like to point out a few of the advantages derived from this manner of presentation:

1. It will lead the physician to an exact and thorough investigation of anamnestic data, which is one of our essential diagnostic aids. One is often surprised at the amount of information missed that has yet to be supplemented while trying to put things on record.
2. It alleviates the work-up of cases and provides ready information about important events and interrelations such as menstruation, gravidity, courses of treatment, et cetera.
3. It is extremely helpful for demonstration.
4. It increases our supervisions and criticism of therapeutic steps that were taken.
5. It can act as a stimulus to draw up similar "Life Lines" for other groups of maladies.

A single case will illustrate the practical application of the A.L.L. (Chart II).

ALLERGY — LIFE — LINE. (A.L.L.)

Name ..... No. .....

Sex: m. f. Origin .....

Age: at first visit ..... Immigration .....

.....

Diagnosis:

Asthma br.

Rhinitis

Poll. All.

Eczema

Urticaria

Migraine

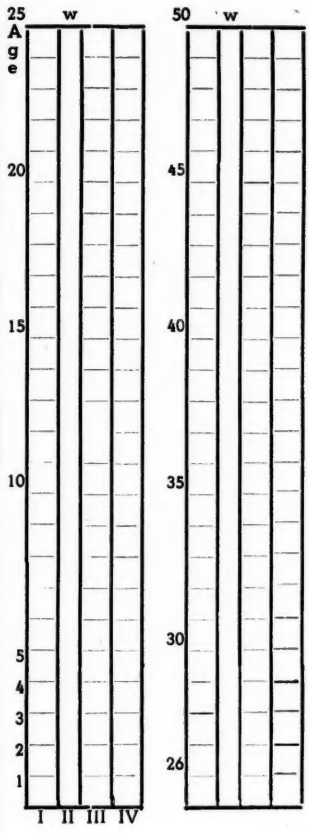
O Ocular

G Gravid

X Protect. Care

? Not known

Remarks:



Dr. M. J. Gutmann
Jerusalem.

Chart I.

ALLERGY — LIFE — LINE. (A.L.L.)

Name A. F. No. 2898

Sex: ~~m~~ f. Origin Austria

Age: at first visit 29(38). Immigration 1936.

Diagnosis: Eczem, Rhin., Asth., Poll.

Asthma br.

Rhinitis

Poll. All.

Eczema

Urticaria

Migraine

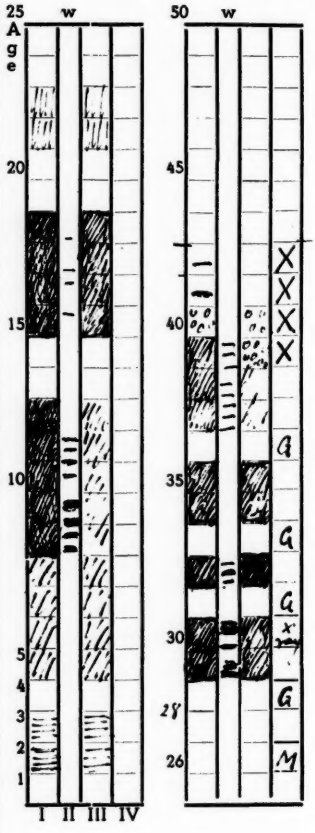
O Ocular

G Gravid

X Protect. Care

? Not known

M MARRIAGE



Remarks:

Heredity:

Father asthma

grandmother m. Ast

1 son Eczem + Rhin.

Dr. M. J. Gutmann
Jerusalem.

Chart II.

ALLERGY LIFE LINE—GUTMANN

A woman 42 years old of European origin immigrated into Israel in 1936. She came to my clinic the first time at the age of twenty-nine, when I saw her only once. There was onset of allergic symptoms (eczema) within one year of age. Rhinitis started at the age of four, and at eight years asthmatic conditions developed and continued until the twelfth year with frequent interruptions of the child's working ability (blocking the "W" line). This was followed by two years during which the patient was free from any allergic symptoms. Between the ages of fifteen and nineteen she was almost constantly suffering from asthma, but with little interference with her work at school. Then followed a long period with no asthmatic attacks. During her twenty-second and twenty-third years, she occasionally suffered from migraine headaches. She married at the age of twenty-six (M) and gave birth to her first child at the age of twenty-eight. Shortly afterwards, heavy asthmatic attacks reappeared with some improvement after x-ray treatment, and disappeared totally during the second pregnancy at the age of thirty-one. There followed a period of severe attacks which were interrupted only during a third pregnancy a year later and the fourth gravidity at the age of thirty-six. Two years later, exactly nine years after I first saw her, the patient came again to my clinic with severe asthma. It was only now that a detailed diagnosis could be made. Pollens were found to be the main cause of her bronchial asthma. Under the protective care ([X]) of a desensitization with pollen extract she recovered remarkably, and for the first time in many years she succeeded in achieving a complete working capacity which could be maintaind until now, her forty-second year.

There is space remaining on the sheet for other important remarks, such as heredity, et cetera.

SUMMARY

A simple graphic representation is drawn up to obtain a swift and intelligible survey of the sequence of allergic events in the patient's life—the Allergy Life Line (A.L.L.)

The advantages of such a representation are described.

PENNSYLVANIA ALLERGY ASSOCIATION

The Spring Session of the Pennsylvania Allergy Association will be held at Pocono Manor, Pennsylvania, May 7, 8 and 9, 1954. Speakers on the program May 8 and 9 will be Drs. M. J. Leitner, Lester Fowle, James Mansmann, Louis Tuft, H. B. Haag, Charles Brown, Mayer Green, Howard Leopold, William Reyer, and Samuel Burden. Dr. Charles Cleland and Dr. Leslie Bartlett will act as Moderators.

NITRATE OF POTASSA, IN ASTHMA

(Historical Document)

TO THE EDITOR OF *THE BOSTON MEDICAL AND SURGICAL JOURNAL*:

Sir,—Knowing that the pages of your Journal are open for communications, I would offer, for the benefit of its numerous readers, a few remarks *upon the use of Nitrate of Potassa, in the treatment of Spasmodic Asthma.* Asthma has been divided, by most writers, into two kinds—viz., nervous or spasmodic asthma, and asthma dependent upon discoverable organic lesions. It is upon the former of these two varieties that I wish to make a few remarks, founded upon personal observation.

Mr. E———, a tradesman of this place, has, for about seven years past, been troubled with repeated paroxysms of asthma, in its most severe form. The paroxysms generally occur suddenly, and after some slight exposure to cold, over-exercise, or the inhalation of impure air, such as that impregnated with dust, smoke, etc.

The appearance of the patient, when laboring under an attack, is very striking. The countenance is as it were blanched, lips livid, extremities cold, pulse small and feeble, and the circulation generally retarded. Upon listening over the region of the lungs during the paroxysms, the sound heard conveys the idea of air being slowly forced through fine net work, at the same time meeting with much resistance. These paroxysms occur, sometimes daily, for a week or more, and then the patient may, by protecting himself from the common exciting causes, be free from them for two or three weeks; but finally they recur with all their accustomed violence. The remedies which at first suggest themselves to the practitioner, are classed under the head of antispasmodics. The most reputed of these have been used in the case under consideration, often at first giving signal relief, but soon losing their power. Next to these, narcotics have been used, but with the same results. Chloroform and ether have been freely inhaled, with no good effect; on the contrary, an aggravation of the paroxysm occurred. The only remedy which the patient can rely upon, is the nitrate of potassa. He has used this very frequently (more than one hundred times) for the last two years, and invariably with immediate relief. The method of using it is as follows: A saturated solution of the nitrate is prepared, and slips of unglazed white paper, nine inches long, and four inches in width, are soaked in this solution for fifteen minutes. These are then folded in a manner to form a piece nine inches long and one inch wide, then dried in an oven, and laid aside for use. Upon the occurrence of a paroxysm, the end of one of these is ignited, and placed in a close room in which the patient is seated. The inhalation of the fumes arising from the burning nitrate affords immediate relief in the most violent paroxysms.

The question may be asked, in what way does the inhalation of these fumes effect this speedy and unequivocal relief? We are informed from the chemist, that 1 pound of the nitrate of potassa will furnish, when heated to redness, more than 400 pints of oxygen gas. If we are to support the

Reprinted from *The Boston Medical and Surgical Journal,* 39:358-359 (Nov. 29) 1848.

theory of Laennec, viz., that spasmodic asthma is dependent upon an increased necessity of respiration, and consequently of oxygen, is it not reasonable to suppose, that the air of the room becoming more highly charged with oxygen from the burning nitrate, the paroxysm is thus relieved? These are questions I would propose for further investigation.—*H.T.E.*

FELLOWSHIP REPORT

The College is pleased to announce the following list of names of those who have been elected to Honorary Fellowship, promoted to Fellowship, new Fellows, Associate Fellows and Corresponding Fellows:

Honorary Fellow

Otto Loewi, M.D., Sc.D. (Hon.), Ph.D. (Hon.), 155 East 93rd St., New York 28, N. Y.

Associate Fellows

Zoltan Bernath, M.D., Santiago, Chile.
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N. John Colombo, M.D., 39 Church St., Hudson, Mass.
Hyman Fogelman, M.D., 1104 Elder Ave., New York City 72, N. Y.
William T. Ford, M.D., 460 Market St., Williamsport, Penn.
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Morton L. Hammond, M.D., 350 N. E. 15th St., Miami, Florida.
Guillermo Manrique de Lara, M.D., Camilo Carrillo 473, Lima, Peru.
Harold Charles Menger, M.D., 259 Brevoort St., Kew Gardens 15, N. Y.
Joseph B. Miller, M.D., 904 Dauphin St., Mobile, Ala.
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Alexander Roth, M.D., 411 Nichols Road, Kansas City, Mo.
Arthur S. Sandler, 1626 Nix Professional Bldg., San Antonio 5, Texas.
Ines Maria H. Santos, M.D., 1419 E. 60th St., Chicago 37, Ill.
Lowell R. Stephens, M.D., 600 East Liberty St., Covington, Indiana.
Elvira L. Wasserman, M.D., 167 Northern Boulevard, Flushing 58, N. Y.
J. Coburn Whittier, M.D., 1128 N. Brand Blvd., Glendale 2, Calif.
Robert B. Zatz, M.D., 1384 Union St., Brooklyn 13, N. Y.

Promotions to Fellowship

Samuel Bloom, M.D., 9538 Kings Highway, Brooklyn 12, N. Y.
Edmund D. Colby, M.D., 855 Union Street, Schenectady 8, N. Y.
Samuel H. Eisenberg, M.D., 1727 S. Main Street, Akron 1, Ohio.
Frank A. English, M.D., 308 W. 2nd Street, Roswell, New Mexico.
Ralph Hale, M.D., 1418 Bryant Bldg., Kansas City, Missouri.
Irvin H. Moore, M.D., 5013 France Ave. South, Minneapolis, Minn.
Arthur H. Sussman, 345 Bloor Street W., Toronto 5, Ontario, Canada.

Fellows (New Members)

Demetrios Anthoulis, M.D., 107 Solonos St., Athens, Greece.
Samuel Dennis Bell, 131 E. 74th St., New York 21, N. Y.
Paul F. deGara, M.D., 876 James St., Pelham Manor, N. Y.
Allan Hurst, M.D., 1578 Humboldt St., Denver 18, Colorado.
Douglas E. Johnstone, M.D., 216 Meigs St., Rochester 7, N. Y.
Jose Martorelli, M.D., Rio Cuarto, Argentina.
Edwin P. Preston, M.D., 518-19 Du Pont Bldg., Miami 32, Florida.
Michael J. Ressetar, M.D., 473 Lexington Ave., Clifton, New Jersey.
Harold S. Tuft, M.D., 304 S. 19th St., Philadelphia, Penn.

Corresponding Fellows

Plutarco Naranjo, M.D., Cali, Colombia.
Professor Umberto Serafini, Rome, Italy.

Case Report

BELL'S PALSY—SERUM OR PENICILLIN SENSITIVITY? TREATMENT WITH CORTISONE

A Case Report

LAWRENCE J. HALPIN, M.D., F.A.C.A.
Cedar Rapids, Iowa

THAT BELL's PALSY may be a part of a reaction picture is exemplified in the following case report. Varieties of conditions, infectious, non-infectious and idiopathic, have been contributing factors to impaired function or paralysis of the seventh nerve. Regardless of the pathological source of irritation, edema of the nerve, the nerve sheath or of the anatomical structures of the bony canal has been credited with being the basic etiological feature. Serum neuritis has been recognized as a prolonged, distressing component of serum reactions. Serum neuritis as a part of penicillin sensitivity must also be given consideration. Since this reported patient had received both antitetanus serum and penicillin, it can be postulated that his subsequent Bell's palsy was founded upon his sensitivity for one of these agents. The response to treatment would lend support to this premise. Previous experience, and a hasty review of available literature, has placed the recovery period in Bell's Palsy from several weeks to several months.

Coincident with this report, Robison and Moss[1] have written of similar instances of therapeutic response. Their patients presented seventh nerve involvement thought to be due to infectious or idiopathic origins. This patient may rightfully be classed as idiopathic, but I prefer to consider it as an integral part of serum or penicillin sensitivity.

Case 1.—A twenty-seven-year-old man, employed as a plumber, stepped on a nail, puncturing the skin of his right foot. The accident occurred November 6, 1953. He was given 1500 units Antitetanus serum and 300,000 units penicillin as part of his emergency medical care. No symptoms nor complaints were experienced until three days later. He then noted the onset of generalized muscular aching, a sensation of chilliness and a recorded elevated temperature of 102° F. Upon the assumption that these findings might be part of a serum or penicillin reaction, his physician prescribed the use of oral cortisone (100 mg. daily in divided dosages) and an antihistaminic preparation (type and dosage undetermined). Such measures were continued for two to three days, and his recovery was apparently complete. Work was missed during this period of acute illness. The patient remained essentially well until November 26, 1953, twenty days after the serum and penicillin administration, when numbness and tingling were noted in the right facial area. Shortly after paralysis of the muscles in this location was apparent.

He was originally seen by this reporter November 30, 1953. On examination, he was unable to close his right eyelids; the attempt to smile or whistle resulted in a marked drawing of these areas to the left, and weeping from the right eye was pronounced. He was unable to wrinkle his forehead on the involved side. There was no evident loss of sensory perception. He had no complaints of alteration in hearing, taste nor smell. There was no complaint of pain nor distress at any time, though the patient was obviously concerned with his condition. The persistent numbness

and tingling were not sources of discomfort. With a diagnosis of Bell's palsy, and in view of his previously administered serum and penicillin, cortisone (200 mg. daily in divided dosages) was instituted on November 30, 1953.

Subsequent visits revealed some improvement within four days as shown by less weeping of the right eye, and a return of partial strength in the right facial muscles. By December 8, 1953, nine days after cortisone administration, the patient was practically normal in his appearance. He had missed no work during this period of paralysis. Cortisone dosage was gradually decreased and eventually discontinued December 15. There has been no recurrence of his complaints on reduced dosage nor has there been any residual findings on subsequent examinations.

COMMENT

Cortisone administration to this patient resulted in prompt recovery from complaints which are notorious for prolonged persistence. From this one instance, no conclusion can be taken that the facial paralysis was a true part of a sensitivity reaction. Highly suggestive, however, is the time of onset in relation to the administration of the serum and/or penicillin. These delayed symptoms are further suggested on this basis by the reaction (?) picture three days after the preventive medication had been given.

The association of Bell's palsy as a finding in serum or penicillin sensitivity is purely hypothetical, but the rapid clearing of the paralysis with cortisone therapy is interesting and noteworthy.

REFERENCE

1. Robison, W. P., and Moss, B. F.: Treatment of Bell's palsy with cortisone. J.A.M.A., 154:142 (Jan. 9) 1954.

808-810 Merchants National Bank Building

THE ACADEMY OF PSYCHOSOMATIC MEDICINE

The program of the first annual meeting of the Academy of Psychosomatic Medicine, to be held at the Plaza Hotel in New York City on October 8-9, 1954, will be devoted to *Psychosomatic Aspects of Surgery*. There will be contributed and invited papers on such topics as: Psychosomatic Aspects of Anesthesia; General Surgery; Gynecological Surgery; Plastic, Otolaryngological and Oral Surgery; Mutilating Operations; Endoscopic Surgery; Orthopedic Surgery; Eye Surgery; Pediatric and Geriatric Surgery; and Neurological Surgery.

Those who are interested in presenting papers should write to Dr. Benjamin Raginsky, 376 Redfern Ave., Montreal, Canada, stating their special interest.

Progress in Allergy

PEDIATRIC ALLERGY

A Critical Review

C. COLLINS-WILLIAMS, M.D., F.A.C.A.
Toronto, Canada
and
BRET RATNER, M.D., F.A.C.A.
New York, New York

This review of the literature continues from the review of pediatric allergy published last year under the same title. Again, not only the papers which have been published referring directly to allergy in children, but also those which refer to adults provided that the subject matter is of interest to pediatricians and pediatric allergists, are reviewed.

DERMATOLOGIC ALLERGY

Tachau[87] in a discussion of infantile eczema stresses that reliance on the skin tests for diagnosis is unreliable and also recommends radiotherapy for treatment in those cases which have not responded to conventional methods. This author's comments on eczema in general are those accepted by most allergists, but the two aspects referred to are rather controversial in as much as many allergists feel that skin tests are of considerable value in the evaluation of a case of eczema, and also many feel that radiation therapy is rarely indicated.

Purdy[59] described an investigation to demonstrate the proportion of children who suffer from infantile eczema, who go on to suffer from asthma, hay fever or childhood eczema, i.e., Besnier's prurigo. This was done by a questionnaire sent to patients. Of the ninety-three patients who could be followed, it was revealed that 50½ per cent had suffered with asthma, 42 per cent with hay fever, 25 per cent with Besnier's prurigo and 7½ per cent with migraine. Of the total of ninety-three patients, sixty-three or a total of 68 per cent had suffered from Besnier's prurigo, asthma or hay fever. Of these, 56 per cent of the total had suffered one of the sequelae of a moderately severe or very severe degree. In other words, approximately 56 per cent of infants who have suffered with eczema are destined to many years or a lifetime of grave disability from sequelae. This study is similar to many others which have been reported. The authors of this review described a follow-up of 750 cases of allergy in children and found 59 per cent of these who had suffered allergic eczema at one time later suffered from respiratory allergy. They called this "allergic dermal-respiratory syndrome."[61] In this article the authors refer to thirteen other series of children presented in the literature which gave an average incidence of both dermal and respiratory allergy in the same patient as about 28 per cent. This article therefore confirms the impression of previous authors.

Ingram[39] has published a general discussion of the treatment of eczema.

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He feels that in these patients there is always a disturbance of emotional and nervous stability and adjustment as a primary cause but there are also external causes such as irritants and allergens and internal causes such as substances taken into the body. He emphasizes the fact that symptomatic treatment should be both simple and rational.

Stoesser and Nelson[84] discuss the use of synthetic vitamin A in the treatment of eczema in children. They treated ten children from six months to ten years of age with 25,000 to 200,000 units of synthetic vitamin A per day for periods of from three to twenty-one months. Of the nine children who tolerated the vitamin, three showed some improvement and six had marked improvement of their eczema. There were no changes indicative of vitamin A toxicity in this series. The difficulty with such a study is that it is the natural tendency for the majority of cases of eczema to show improvement under treatment and, therefore, it is difficult to accept the claim of the authors that the improvement in these children was due to the vitamin A. Also there have been a great many cases of poisoning by vitamin A reported in the literature from doses which were not in excess of those used by these authors. Therefore, one must regard this method of therapy as a potentially dangerous one even though the authors did not observe any toxicity.

Brown and Holman[8] describe nine patients with eczema varying in age from twenty-three months to eleven years, all of whom had generalized eczema, all of whom were hospitalized and all of whom were put on a diet with a complete substitution of goat's milk for cow's milk. All patients had a negative scratch or patch test to cow's milk. The authors did not find any effect on the course of eczema by the substitution of the goat's milk for cow's milk. However, goat's milk could be expected to benefit a patient with eczema only if the patient were sensitive to the lactalbumin of cow's milk because the lactalbumin of goat's milk is different from that of cow's milk. If the patient is sensitive to casein the casein is similar in the two milks and therefore goat's milk would not be expected to benefit the patient. These nine cases showed no evidence as far as is given by the authors of being allergic to milk in any form. Therefore, the study is very inconclusive as to whether goat's milk is ever of any value in eczema. From a practical point of view, most children who are allergic to milk, can tolerate evaporated or heated evaporated milk without difficulty because most of the sensitivities are due to the albumin fraction and the albumin is denatured by the process of heat. In some very sensitive children who are sensitive to the lactalbumin of cow's milk, it is possible that goat's milk would be of benefit even though evaporated cow's milk does cause symptoms.

Diamond[22] has published another paper emphasizing the importance of inhalant allergens in the etiology of atopic dermatitis. He reports 236 consecutive new cases seen by him; the primary complaint was directed towards the respiratory tract in 179 of these cases and among these the diagnosis of a concomitant atopic dermatitis was made in twenty-three instances or 9½ per cent of the total. In the remaining fifty-seven cases, the primary complaint was of a dermatological nature and of these more than one out of four of the cases had respiratory symptoms caused by inhalant allergens. He found that patients with dermal allergy frequently showed improvement of their dermal allergy coincident with treatment of the respiratory complaints by means of individual extracts, and he found that small doses of extracts were much better for treatment of these patients

than large ones. He also found exacerbations of dermatitis caused by the inhalants following the injections of extracts for the purposes of testing or for therapy. He gives several case reports to support the view that both the dermal and respiratory allergies were due to the same inhalant allergens. Of these patients only one is a child but the same findings obviously refer to both children and adults. In the opening statement of his paper, he points out that it is generally believed that inhalant allergens such as house dust, pollens or molds are very rarely involved as causative agents in atopic dermatitis. While one must admit that this belief is found among the profession at large, it is very difficult to see why it should be, since so much has been published on this subject in the past few years and the etiologic relationship of inhalant allergens to atopic dermatitis has been definitely proved in so many reported cases. It is high time that the profession at large was aware of this fact.

Tuft and Heck[88] have published an additional paper on this same subject, this one dealing with the importance of ragweed in the etiology of atopic dermatitis. They studied 136 patients, sixty-eight of whom were children, with atopic dermatitis. Of these, 121 gave positive reactions to ragweed. This proportion corresponded roughly to the incidence of positive pollen reactions seen in hay fever patients in the area, whereas in a control group of 100 consecutive patients with allergic conditions in which pollen was not likely to be a factor there were only 5 per cent positive reactions to ragweed showing that the high incidence of reactions to seasonal inhalant allergens in atopic dermatitis was not a normal reaction and could not be a matter of accident or coincidence. Sixty-four of these 121 patients had an associated ragweed hay fever and/or asthma. In thirty-six of the sixty-four patients, the dermatitis occurred in the ragweed season or was perennial with seasonal aggravation. In other words, the positive ragweed reaction could be accounted for upon the basis that it was the cause of both the hay fever and the dermatitis. In the remaining twenty-eight patients with both hay fever and atopic dermatitis, the positive ragweed reaction could be explained upon the basis of the associated hay fever, the dermatitis in such instances being provoked by other allergenic agents. In twenty-three of the fifty-seven patients who had no associated hay fever, ragweed was determined as being of etiologic significance in the causation of the atopic dermatitis but in the remainder the positive ragweed reaction was still unaccounted for. However, some of these cases were followed long enough that hay fever was seen to develop in the ragweed season a few years after the positive skin test was obtained so that it was quite possible that many of these positive unexplained ragweed reactions were of future clinical significance. Thus, there was a total of fifty-nine patients of the 121 in whom pollen sensitivity was definitely related etiologically to the dermatitis. To further substantiate this claim, two patients were given repeated inhalations of ragweed pollen through the nose and dermatitis was produced. In sixteen other patients the dermatitis was induced by the injection of ragweed pollen extract given for purposes of desensitization. That this was specific was indicated by the fact that it did not follow the injection of a buffered saline solution used as a control. Thus, the authors have presented evidence, both clinical and experimental, which proves that seasonal inhalant allergens as represented by ragweed pollen are important inhalant factors in the etiology of atopic dermatitis, and it is reasonable to assume that these conclusions can be applied to other pollens and to atmospheric molds.

Owings and Riley[55] studied the electrolyte levels in the serum of infants

during the first two years of life during the exudative phase of infantile eczema. Twenty out of twenty-two consecutive cases had an elevation of the serum potassium which was elevated in proportion to the total area of exudation and to the acuteness of the process. Sixteen had an elevation of the serum sodium and four additional patients had a high normal serum sodium. Serum phosphorus levels in five patients tended to fluctuate similarly to the serum potassium. With improvement of the eczema, the electrolyte levels tended to revert to normal. The authors suggest that these electrolyte changes may represent potassium and phosphorus mobilization and loss with sodium retention and subsequent water logging of the shocked organ.

Rook and Frain-Bell[69] report 100 consecutive cases of papular urticaria, varying in age from two weeks to seven years, but 89 per cent of cases occurred under three years. Sixty-two per cent were affected more severely during the summer. In the majority, the legs and lower trunk were principally involved, and in 32 per cent another member of the family was affected. The lesions consistently cleared when the child was admitted to a hospital but new crops of lesions frequently recurred within a short time on his return home. They found that in some cases the response to the use of 5 per cent D.D.T. in talc as a dusting powder was quite dramatic. In others, it produced only a partial cure and in a few it was of no benefit. They conclude from their own series and from a review of the literature, that most if not all cases of papular urticaria are the result of an acquired sensitivity to certain insects, especially fleas and bed bugs.

King and Forrest[42] report the case of a six-year-old girl who, following vaccination on her arm, developed vaccinia of the eyelids, the diagnosis being proven by animal inoculation and cultures. The response to aureomycin was dramatic. They report knowledge of two other patients with vaccinia involving the eyes, one with corneal complications who also responded well to treatment with aureomycin. Although the reported case was not an allergic patient this disease is of course most commonly seen in eczematous infants and therefore knowledge of its treatment is essential to the pediatric allergist.

Baer and Leider[3] published a report on progress in dermatologic allergy, a critique and review of the literature of 1951-1952. This paper is itself a review and will not be further discussed here.

RESPIRATORY ALLERGY

Buffum[11] reviews the records of thirty private patients seen with the diagnosis of asthma before one year of age. These patients were completely studied and the author concludes from his study that these patients suffer from extrinsic asthma due to inhalants and to foods and that the infectious element is of secondary importance. Although in many cases the attacks are precipitated by respiratory infections it seems most likely that the babies with negative skin tests are also allergic to inhalants and foods and that the respiratory infection is an additional precipitating factor. This fact, which is accepted by most allergists, is of course of extreme importance in the treatment of infants in this age group with asthma.

Stevens[82] describes a few carefully selected patients, one group who had asthma appeared to be sensitive only to bacteria; a second group who had asthma were sensitive to relatively few allergens including ragweed. However, the second group had asthma with colds though they did not show positive skin test with bacteria. All of these patients were children. The

purpose of the paper is to show the difference between these two groups of patients. The first group comprised of nine patients, all under seven years of age when first seen, had had febrile winter colds with asthma for from one to four years previous to the first examination. In all of them the attacks were worsening. Each patient gave several positive skin tests to the most commonly reacting allergens but since they had no asthma between colds and during the summer it was believed that they were not clinically sensitive to these substances. They did, however, have attacks of asthma after colds during the winter time. The patients were desensitized with mixtures of bacterial filtrates for two or three years and all of them showed considerable improvement, many of them being relieved entirely of their asthma. The second group comprising seven patients had had asthma due to various foods and inhalants. At the time they were seen they were all sensitive to ragweed which was etiologically responsible for their asthma. They gave negative skin tests to bacteria and in these patients desensitization with bacterial filtrates was not necessary, inoculations with ragweed alone having been adequate, unless the asthma occurred with colds throughout the winter. The author believes that in this group the irritating and inflammatory effects of the infection initiate the attack of asthma and that primary bacterial sensitivity is not responsible. The case reports in this paper are quite convincing, showing the two groups into which children who have asthma associated with colds can be divided, and the response to the therapy of one group without bacterial vaccines and the other group with bacterial vaccines is also very convincing. However, it happens very frequently that a young child who is completely tested with the various allergens may give all negative reactions to them even though he is having severe asthma, but if he is followed, he subsequently, perhaps a few years later, will give positive reactions to many allergens which can be identified as being etiologically responsible for his asthma. Therefore as the child grows older, it is not always possible to put him categorically into one of these groups or the other. Actually, it is the experience of the authors of this review that all children with respiratory allergy do better if respiratory vaccines are included in their hyposensitization program, whether or not they show positive reaction with bacteria by skin tests.

Mansmann[48] reviews the factors used in the etiologic diagnosis of bronchial asthma. Since this is itself a review it will not be further discussed here.

Mears, Prickman and Moersch[50] discuss bronchostenosis as a complication of asthma. They define bronchostenosis as a definite stricture-like narrowing of a bronchus that is considered to be inflammatory in nature and not the result of allergic edema or spasm and state that in either intrinsic or extrinsic asthma it is often unrecognized. They review the records of 1,034 consecutive asthmatic patients who underwent bronchoscopic examination and in these 227 were found to have stenosis of one or more bronchi. The patients varied in age from three to seventy-four years; fifteen were nine years or younger, while the majority were in the decade from forty to forty-nine years inclusive. The syndrome of bronchostenosis complicating asthma is a rather definite one. The most prominent symptom is cough which is usually persistent and at times paroxysmal, usually productive of sputum. Localized obstructive pneumonitis may develop and persist until the site is drained. The second most common symptom is fever usually accompanied by leukocytosis. Hemoptysis is seen frequently. Half of the patients gave a history of infec-

tion of the upper respiratory tract preceding the attack of asthma. A history of one or more episodes of pneumonia was obtained in 43 per cent and a positive history of pleurisy on the affected side in 32 per cent. It should be axiomatic that a patient who has asthma and experiences one attack or repeated attacks of pneumonia or pleurisy should be suspected of having bronchostenosis until the nature of the illness is proved otherwise. Physical examination may disclose no abnormal findings other than the usual asthmatic râles. However, additional abnormal findings, usually those of obstructive pneumonitis, may be found. In only one-third of cases were thoracic roentgenograms of value in making a diagnosis of bronchostenosis. The authors feel that the most common indication for bronchoscopic examination in patients with asthma is the need of confirming or excluding the diagnosis of bronchostenosis. The treatment of bronchostenosis consists of dilatation of the stenosed bronchus and aspiration of the retained secretions. Patients treated in this way receive a lasting benefit from dilatation and aspiration. This paper is important because it draws attention to the complication of asthma which is infrequently thought of and recognized.

Black et al[4] report on a nine-year-old girl who was studied in a Pediatric and Allergy Clinic for a period of several months with a diagnosis of bronchial asthma. After several months she coughed up a shell of a pistachio nut after which her so-called asthma disappeared. The authors point out the difficulty of these cases in which foreign body simulates asthma and emphasize the need for very careful exclusion of foreign body as the cause of the symptoms. This paper draws attention to another very important cause of wheezing which must be carefully differentiated from allergic asthma. This should be thought of in every case of wheezing, especially if there has been a history of sudden onset, or if there is an associated unresolved pneumonia. This is another reason for never undertaking the treatment of a patient with asthma unless a chest x-ray has been taken.

Siegal et al[75] discuss recent advances in the treatment of bronchial asthma based largely on their own experiences. They discuss pulmonary function studies; symptomatic relief of the attack; the value of bronchoscopic suction; the therapeutic use of gases and aerosols, including a discussion of carbon dioxide intoxication syndrome, the management of infection and therapy with ACTH and cortisone. They also describe the uses of several new medications which have just appeared on the market.

Fein et al[28] discuss respiratory exercises as an ancillary treatment in bronchial asthma. The authors used the respiratory and physical exercises as outlined by the Asthma Research Council of London, England. They studied thirty cases in all. Group 1 contained five patients who were followed in the allergy and physiotherapy departments at biweekly intervals for one year and had their exercises under strict supervision. In this group 100 per cent of cases were able to increase the chest expansion in the upper chest, 60 per cent were able to increase expansion in the upper and lower chest, 60 per cent were able to learn control of diaphragmatic breathing and 60 per cent of cases were able to abort mild paroxysms of asthma. Group 2 consisted of ten patients who received four supervised exercise periods and subsequently conducted their exercises at home without supervision. In this group 60 per cent were able to increase chest expansion but none were able to master control of diaphragmatic respirations. Group 3 had fifteen patients who were treated in the Allergy Clinic with desensitization treatment but no exercises. This group showed no permanent

change in hemithorax measurements or ability to improve the chest expansion. The authors feel that these treatments require special supervision which is most readily available in institutions with physiotherapy departments. This paper draws attention to a very rational ancillary treatment of bronchial asthma and one which, on this continent at least, is considerably neglected. While this series is so small that it cannot be concluded that the results of exercises are always advantageous to the patient, nonetheless it would be well worth while for several large series to be run to properly evaluate this procedure rather than discarding it without trial as is done in most clinics.

Dees et al[20] studied the value of nephenalin, an orally administered combination of rapid and prolonged acting bronchodilators in asthmatic children. For their study, the authors used this drug in the treatment of the acute asthmatic attack in fifty children over a clinical trial extending from three weeks to one year. All children had moderately severe to severe asthma. They found that the combination gave effective relief in approximately 66 per cent of the children. It was relatively free from unpleasant side effects, only four children experienced any symptoms which made them reluctant to continue with its use, and no harmful effects were noted in any child. Thirty-eight per cent found this preparation the most effective medication they had used for asthma.

Unger and Unger[89] studied the use of Tryptar (Trypsin) in bronchial asthma and other respiratory conditions. They administered the drug 312 times by aerosol in eighty-one patients with bronchial asthma and other respiratory conditions. Inhalations were very effective in removing thick sputum which the patient was unable to expectorate. In chronic bronchial asthma with emphysema the results were disappointing; much greater relief occurred in a few patients with paroxysmal bronchial asthma, and spectacularly excellent results occurred after inhalations were given to patients with bronchial asthma plus some pulmonary infectious process and with bronchiectasis. In atelectasis the results were also spectacular. They conclude the Tryptar aerosol is a safe procedure and hoarseness, the only troublesome side effect, is infrequent if care is used.

Gottlieb[34] reviews the recent literature on bronchial asthma.

Malloy[47] reports seventy-eight cases of ragweed hay fever; the patients varying in age from six to sixty-six years, were all treated by hyposensitization therapy. Eight patients were given perennial treatment and the remaining seventy were given pre-seasonal treatment only, beginning about March 20 or later and receiving twenty to twenty-five injections. Of these patients, fifty-six received a dosage schedule which contained less than 1,000 protein nitrogen units as a final dose. Ninety-five per cent of these patients did poorly. In the remaining twenty-two cases the patients received more than 1,000 protein nitrogen units as a final dose, and 86 per cent of these patients did well. The author, therefore, concludes that there is, in the treatment of ragweed hay fever, a critical level of dosage above which one may expect to get good results and below which results are almost uniformly poor; that all ragweed hay fever patients should be treated with dosage schedules, the final dose of which contains at least 1,000 protein nitrogen units. This appears to be a very carefully done piece of work. However, proponents of the low dosage method of hyposensitization would find it difficult to believe that such high dosage is really necessary. Both the authors of this review, for example, use a low dosage method where the top dose is 0.15 cc of a 1:5,000 dilution of the positively reacting inhalants, pollens and molds and in the case of rag-

weed such a top dose would include approximately 19 protein nitrogen units of ragweed which is far below this author's recommended dose of 1,000 units. However, there are certain differences between these two groups of cases. Malloy's cases were largely adults and presumably most of them were ragweed cases. All of his cases were treated for only the one season, the conclusions drawn based on the results of that one season, and most of his cases were treated by only the preseasonal method. The authors of this review on the other hand, use almost entirely the perennial method of treatment, all of their cases are children and their conclusions on good results, which are approximately 90 per cent, are based not on the first year of treatment but on the first few years of treatment. Moreover, many of the cases react to a great many other inhalants, pollens and molds and these are also included in the same hyposensitization program.

ACTH AND CORTISONE

Brown[10] reports on the use of ACTH and cortisone in the treatment of forty-seven patients with severe allergic diseases: twenty-nine with intractable asthma, eleven with intractable dermatitis, four with urticaria and angioneurotic edema, two with hay fever and one with chronic allergic sinusitis. Good results were obtained in forty-three cases, four were classified as failures. He stresses once more that this is only for temporary relief and that the usual anti-allergic therapy must be followed for permanent benefit to the patient.

Hampton[36] reports on the treatment of sixty cases of asthma, urticaria and allergic dermatitis with ACTH intravenously alone, or by combined intravenous and intramuscular methods. He feels that ACTH intravenously or combined with intramuscular administration has a great advantage over the conventional intramuscular use of the hormone, but again emphasizes that effective relief is on a temporary basis only.

Hill[38] discusses the oral treatment of infantile eczema with cortisone. He feels that treatment with cortisone by mouth has a very definite place in eczema. Short term therapy with large doses is of little practical value except for periods of extreme emergency, but long term therapy with smaller doses is a worthwhile procedure in certain cases. He treated eighteen infants under the age of three years with oral cortisone. In most of the cases the eczema was severe, some of the patients having done poorly with the usual methods of treatment. In all cases but one, the maximum dose of 75 mgs of cortisone per day was adhered to, and in addition to the cortisone each patient was treated as he would have been if cortisone had not been used. In four cases the results were unsatisfactory, in six they were worthwhile but not superior and in eight cases the results were superior. The author stresses that if infantile eczema is to be treated with cortisone at all it must be treated with a dosage that does no harm—he saw important side-effects in only two cases. He feels that if eczema is entirely controlled with 75 mgs or less, cortisone should be continued at this level, but if it is not entirely controlled with that amount he does not feel that a larger amount should be used. In his opinion it is best to start with 75 mgs, and as soon as the eczema is controlled to reduce the dosage by 12½ mgs each day to determine what daily dosage is necessary for that patient. He stresses that cortisone is only symptomatic treatment. The presence of skin or respiratory infection is not necessarily a contraindication to the use of cortisone provided that the child is seen frequently and that antibiotics are given. If

during the course of treatment a surgical operation is necessary, it is of the utmost importance that the dose be increased by at least 50 per cent before and for several days after the operation. When cortisone is discontinued this should not be done abruptly. It is possible to continue cortisone treatment for several months without apparent harm to the child.

Sulzberger et al[85] report sixty-two selected dermatologic patients treated by local inunction with hydrocortisone acetate in various ointment bases. Of these 30 were cases of atopic dermatitis and only these will be discussed here. Six of the thirty patients were children. In twenty cases there was definite improvement, in seven no improvement and in three it was questionable whether or not improvement was due to the ointment. When improvement occurred it usually occurred in the first week of treatment, often in the first twenty-four to forty-eight hours. Improvement was usually maintained during the entire time the ointment was being used, the longest observation period being for thirty-five weeks, but when medication was stopped therapeutic effects usualy wore off within four to five days. In most of the cases, improvement was more than 75 per cent, but there were occasional flare-ups even on continued use of the ointment. The authors point out that their findings are in contradistinction to the general lack of effect of cortisone acetate applied locally. They do not believe that there is any serious contraindication to the continued use of the 1 per cent ointment on small body areas up to about one-eighth of the total surface for periods as long as eight months. They did not observe any toxic effects.

Burrage and Irwin[12] report forteen adults who were treated for asthma with cortisone. These were very severe asthmatics of whom many had not responded to the usual methods of therapy. The authors found that the dosage required to control varied considerably from patient to patient but that it was necessary to give a sufficient dosage to render the patient absolutely symptom-free at the outset and then maintain him on small doses. No patient could be kept free of asthma on less than one 25 mg daily dose of cortisone. They stressed that the usual management of bronchial asthma is necessary as cortisone has only a very temporary effect.

Lowell et al[45] report nineteen patients with severe bronchial asthma who were treated with cortisone for a year or more. Two of these patients were children. Seventeen of the nineteen patients maintained a satisfactory state of health but there was no evidence that the underlying pulmonary disease had been materially influenced by treatment. Two patients improved initially but increasing asthma developed under treatment and were considered as failures. The authors found that recurring respiratory infections were difficult to recognize when the patient was receiving cortisone and were often associated with relapse or exacerbation of the asthma.

Schiller and Lowell[73] described fifty-one patients with hay fever, ten complicated by seasonal pollen asthma, who were treated with oral cortisone during the pollen season. All of these patients have been treated unsuccessfully with injections of pollen extracts, antihistaminic drugs, et cetera. The daily dose of cortisone was 100 mgs given in four equally divided doses at six hourly intervals and the course of treatment was for four days. Forty-two of the fifty-one patients were relieved, twenty-five completely and seventeen satisfactorily. Improvement was apparent in most cases within one to two days following the initial dose of the drug. Many of the patients suffered a relapse within seven days after discontinuing the drug. Early experience by these authors showed that the antihis-

taminic drugs gave similar results, namely that about 80 per cent of the patients with hay fever obtained relief. However, the relief and persistence of relief was more marked in the series of cortisone-treated cases.

Moeschlin et al[53] studied experimentally the influence of ACTH and cortisone on experimental antibody production in rabbits, using the agglutinin production caused by the intravenous re-injection of typhoid, paratyphoid vaccine. They found that when ACTH and cortisone were given simultaneously with the intravenous re-injection or up to two hours before the intravenous re-injection, there was no effect on either the quantitative formation of antibodies or the number of plasma cells in the spleen, but when the ACTH or cortisone was started seven days before the intravenous vaccine re-injection there was a marked decrease in antibody production and also in the absolute number of plasma cells in the spleen. However, they feel that this latter is due not to a direct depression of antibody formation but to an inhibition of absorption and degradation of the bacteria into the antigen components. This paper is another contribution to answer the question of the effect of long-term ACTH and cortisone therapy on antibody production in both allergic and non-allergic patients. However, a great deal more work needs to be done before the answer to these questions is found.

Friedman[31] studied the effect of cortisone and hydrocortisone on the production of circulating antibodies in human beings, the antibodies in question being anti-typhoid H and O agglutinins, following the injection of typhoid vaccine. There were five controls who did not receive any hormone, five patients who received cortisone acetate and one patient who received hydrocortisone acetate. Five of the hormone recipients were asthmatics, the others had allergic rhinitis, the controls were all asthmatics. The cortisone or hydrocortisone was given for a full week following subcutaneous injection of the typhoid vaccine on both the first and twenty-second days of the experiment. The anti-typhoid H and O agglutinin titres were measured at the outset and weekly thereafter for six weeks. The author found a marked variability of both anti-typhoid H and O titres within the groups, but there was no greater variability in titres between the hormone patients and the controls than within either group. He concludes therefore that within the limits of his experiment, the hormone has no effect on antibody production but points out that his results are inconclusive because of the few cases studied. It would be worthwhile and necessary to do a great many similar studies, using several different kinds of antibodies, before we will arrive anywhere near an answer as to the effect of ACTH and cortisone on antibody production in the human.

ALLERGY TO PENICILLIN

Siegal et al[79] review the literature on penicillin anaphylaxis and report three new cases, all in adults, one of whom suffered fatal anaphylaxis and two near-fatal anaphylaxis, following intramuscular penicillin in each case. The authors point out that all four fatal cases of penicillin anaphylaxis previously reported, including their own, were patients with bronchial asthma. As to the prevention of penicillin reactions, they point out that penicillin should be used only when there is a real indication and not for minor respiratory infections. The drug is safer given by mouth because, although penicillin sensitization may occur, the recurrence of anaphylactic shock is reduced and anaphylactic deaths perhaps could be prevented completely. Before penicillin is given, a careful history of previous sensitivity should be taken as well as a history of other allergies. Anaphylactic

shock to penicillin need not be feared in patients who have never been exposed to the drug previously. Anaphylactic shock has not been observed after single injections of penicillin during the course of continuous therapy, but have all occurred in patients who have been receiving the drug intermittently. Delayed reactions, which occur after an incubation period of seven to twenty-eight days, of the serum sickness type are usually associated with only a transient period of sensitization and such patients will often tolerate penicillin at a subsequent date without any difficulty. However, in patients who have suffered an accelerated or immediate reaction, the drug is much more dangerous and subsequent administration may result in anaphylactic shock. Skin tests are difficult to interpret and a negative skin test does not rule out penicillin allergy. It is therefore safer to avoid penicillin therapy in patients with the history of an immediate or accelerated reaction despite negative skin tests. Another method of avoiding anaphylaxis is to divide the dose giving a very small amount initially to see if any reaction occurs, and also injecting the penicillin at a site where a tourniquet can be applied if necessary.

Feinberg et al[29] review the literature on both fatal and non-fatal cases of penicillin anaphylaxis and also report nine new cases, four of whom showed non-fatal anaphylaxis and five of whom had fatal anaphylaxis to penicillin. In all five fatalities, postmortem examinations were done. The authors point out that in the anaphylactic reactions the route of administration of the drug has usually been intramuscular although several severe and near fatal reactions have been described as intranasal instillation, aerosol instillation and oral administration. There is a cross reaction between the various types of the drug so that a patient who is sensitive to one type of penicillin may also react to another type. Most of the patients who have suffered from anaphylactic reactions to penicillin have had the drug several times before. In a discussion of skin tests the authors state that it is practically certain that skin tests will be positive in all those persons who react anaphylactically to penicillin. They describe their own technique of skin testing and also discuss the prevention of serious immediate reactions and the treatment of reactions if they do occur.

Mayer et al[49] report six cases of anaphylaxis following the injection of penicillin, all in adults. The patients had received previous penicillin therapy, and four of the six had histories of prior penicillin hypersensitivity reactions. Intradermal skin testing with penicillin gave an immediate wheal type of reaction in two of the three cases in which it was done and in the third patient an almost fatal constitutional reaction developed from the skin test. Passive transfer demonstration of circulating reagins for penicillin was successful in four of the five cases studied. The precipitin reaction was uniformly negative. The authors claim that in all cases of acute anaphylactic-like shock due to penicillin hypersensitivity reviewed in the literature, the immediate wheal type of skin reaction to penicillin was positive when the test was performed. They claim therefore that all patients about to receive penicillin therapy should be questioned about receiving the drug in the past and in the event of a positive or questionable history of penicillin hypersensitivity, skin testing with a high dilution of penicillin should be done. In the event of a positive immediate skin test penicillin is either contraindicated or is given as a calculated risk warranted by the seriousness of the present condition.

Wofford[92] reports one case of non-fatal anaphylaxis to penicillin and states thirty-four anaphylactic reactions to penicillin have been reported in the literature with six deaths. His patient was a nineteen-year-old woman

who had received penicillin on several occasions previously and went into anaphylactic shock following 300,000 units of penicillin intramuscularly.

Sohval[80] reports one severe reaction to penicillin in an adult who had received penicillin several times previously. On the third injection, for an acute illness, he suffered from an immediate anaphylactic-like reaction and recovered in fifteen minutes without therapy.

Pick and Patterson[57] report one case of fatal anaphylactic shock to penicillin in a thirty-one-year-old woman who had suffered from bronchial asthma. She had received penicillin on previous occasions. At the time of her fatal illness, she had an immediate transient reaction following an intramuscular injection and the next day upon receiving the same dose had an immediate anaphylactic reaction which resulted in death. An autopsy was done.

Editorially the Lancet[26] comments on reactions to penicillin and warns against the indiscriminate use of the drug. It quotes a report of the Ministry of Health in England showing that from a limited survey 4.3 per cent of nurses working under local health authorities and 1.8 per cent of nurses working in hospitals have become sensitized to one or more antibiotics. Most of the sensitivities were evidenced as skin lesions.

Editorially the New England Journal of Medicine[24] comments on the same subject referring to a report of the Council of Pharmacy and Chemistry of the American Medical Association on several severe anaphylactoid and fatal reactions to neo-penil. This report indicates that in a period of six months, fourteen severe anaphylactoid reactions including three fatal ones followed the administration of this drug. In nine patients, the reaction occurred almost immediately or within five minutes of injection but in one case convulsive seizures began ten hours after the administration of the drug.

Chotkowski[14] and Fein[27] each report one of these cases of anaphylactoid reaction to neo-penil. Chotkowski did scratch tests on his patient with aqueous penicillin G, neo-penil, and syrup of hydriodic acid and all were negative. Intracutaneous tests were not done. However, subsequently his patient tolerated a small injection of penicillin G and subsequently withstood several doses of penicillin without any reaction. The author concludes therefore that his patient had become sensitized to iodine in the form of syrup of hydriodic acid used as an expectorant and that the anaphylactoid reaction was due to the intramuscular injection of this iodine radical.

Weiss[91] reports a thirty-year-old woman who had received penicillin on many occasions and on the last occasion before the penicillin was given in the present report, she received oral penicillin and suffered mild tingling of the palms of the hands and soles of the feet and vulvar region. On the occasion of the report, she was given penicillin topically into an antrum and within a few minutes had an acute anaphylactic reaction. She had no history of allergy. The author reports that there are two similar cases in the literature.

Blanton and Blanton[5] describe an unusual case of penicillin hypersensitivity in a man who had received penicillin by injection on many occasions without reaction. When he took some penicillin orally he suffered a violent anaphylactic shock. Subsequent to this he had the initial symptoms of shock when he was in a building in which a patient was receiving penicillin aerosol in another room about thirty feet away. He had the same symptoms when he was in a drug store while a druggist was changing penicillin tablets from one bottle to another. Patch tests with penicillin produced large reactions.

Boger et al[6] in the form of a panel discussion, cover pretty thoroughly the field of allergic reaction to penicillin. First are briefly reviewed some of the common reactions to penicillin; namely, the serum-sickness type of reaction, the id type of reaction, dermatitis medicamentosa and contact dermatitis. Next they discuss the uncommon types of reaction; namely, purpura, both non-thrombocytopenic and thrombocytopenic, hematuria, persistent serum sickness-type of reaction, diseases simulating the collagen diseases, obliterative arteritis, generalized periarteritis nodosa, photosensitivity, lupus erythematosis, angioneurotic edema with obstructions of the airways, exfoliative dermatitis, syncope, collapse and death. Convulsive reactions due to intrathecal penicillin are also discussed. Next is discussed penicillin anaphylaxis, fatal and non-fatal. Concerning anaphylaxis to penicillin the following points are noted: (1) anaphylaxis occurs only in those who have had penicillin previously, usually on several occasions; (2) anaphylaxis can occur even though penicillin was well tolerated previously; (3) it occurs more frequently in allergic individuals and is more likely to be fatal in asthmatics; (4) the dangerous and potentially shocking dose is usually the first injection following a prolonged interval since the last exposure to penicillin. The following precautions are suggested for the prevention of anaphylaxis: (1) avoid needless sensitizations by not using penicillin for trivial or doubtful indications; (2) for mild infections employ oral penicillin which is less likely to cause fatal reactions; (3) a careful history as to previous penicillin treatment and reactions is important; (4) the initial or potentially shocking dose should be given into the arm rather than into the buttock so that a tourniquet may be applied. Intravenous penicillin should be avoided. It is wise to inject the first drop or two and then pause for forty-five seconds before completing the injection as the really violent reactions may become evident within seconds. Epinephrine should be readily at hand when giving the injection of penicillin. (5) Preliminary skin tests may be helpful in screening out some individuals who may react with anaphylaxis. Dr. Siegal believes that a simple scratch test should be done routinely and it is best to wait at least fifteen minutes before a final reading. Intracutaneous tests may be dangerous and are best carried out only after a negative scratch test. Since allergy and even anaphylaxis to penicillin may occur in the absence of a positive skin test, an additional helpful precaution might well be the oral administration of a 50,000 unit penicillin tablet ten minutes before the intramuscular injection. Dr. Schiller next discusses his own technique of performing the skin test with penicillin. The scratch test should be used initially. A negative reaction does not rule out the possibility of a serious reaction nor does a positive one indicate that an immediate systemic reaction or even a reaction of a delayed type will ensue. A positive scratch test in an individual with the history of having had one or more courses of penicillin, or one suggesting an allergic reaction from penicillin, is indicative of clinical sensitivity and the likelihood of a severe reaction should penicillin be given. Likewise, the immediate positive intracutaneous test should suggest the existence of a high degree of penicillin allergy. Patients with a delayed type of positive reaction are not as likely to have manifestations of the immediate type. If clinical sensitivity develops at all it will take the form of the more common urticaria or serum sickness type of reaction. As far as the delayed urticaria type of reaction is concerned, Dr. Sherman does not believe that any skin test is of value. Often during and immediately after the delayed urticarial reaction intracutaneous tests are completely negative. However, Dr. Siegal and Dr. Boger believe that the delayed test

does actually indicate the existence of penicillin allergy. Next, Dr. Sherman discusses the basic immunology of the reactions, pointing out that in many ways penicillin reactions are similar to serum sickness due to foreign serum but in many ways are different. Dr. Boger presents statistics showing a low incidence of positive penicillin skin tests in a group who have received no known penicillin therapy, a higher incidence in a group who have received previous penicillin therapy and a very high, over 50 per cent positive reactions, in a group who had known reactions to penicillin. He concludes therefore that one's past exposure to penicillin does have some bearing on the skin sensitivity. The newer types of penicillin are discussed, particularly those which have another radical in the molecule. It is pointed out that all new penicillins represent a chemical union of two drugs and as such the potentials of sensitization are increased; also that all combinations of penicillin with other drugs increase the likelihood of the patient becoming sensitized to one or all of the components. Dr. Schiller next discusses inhalation tests, using penicillin as an aerosol, as a test for sensitivity, and finally the treatment of penicillin reactions with antihistaminics, ACTH and cortisone is discussed.

Collins-Williams and Vincent[16] discuss sensitivity reactions to penicillin in children. They point out that the incidence of reaction to penicillin, as reported in the literature, varies from 2 to 10 per cent, and in table form list the various types of reactions which have been reported. The most common reaction is the delayed serum sickness reaction. They next tabulate the fourteen fatal anaphylactic reactions to penicillin which are recorded in the literature, briefly report on two more which had not been previously reported, and point out that there are many others which have occurred and have not been reported in the literature. Brief reviews are then made of the different types of penicillin reaction which occur; the method in which sensitivity may be developed; the effect of the route of administration of the drug on the development of sensitivity to penicillin; a discussion of sensitivity due to the different types of penicillin available, and a discussion of skin testing. In an attempt to assess the incidence of penicillin sensitivity in children, they made a search for reactions to penicillin at a large children's hospital to which there were 18,000 indoor admissions and 83,000 outpatient admissions each year, and where penicillin was used in large quantity. They could find only three reactions which could be definitely attributed to penicillin sensitivity, although there were five other probable reactions and seventeen possible reactions which could not be substantiated by study of the hospital records. To further assess the incidence of penicillin sensitivity, the charts of 600 private patients were studied, 515 of whom were non-allergic patients and eighty-five allergic patients suffering from a major allergy; ages varying from birth to the fifteenth birthday. In this group, it was found that in the non-allergic children only 0.6 per cent had suffered from definite penicillin reactions, whereas in the allergic group 6 per cent had suffered from definite penicillin reactions. In an attempt to clarify penicillin skin tests, 200 children were tested by scratch and intracutaneous tests with different concentrations of aqueous crystalline penicillin. Two-thirds of the group were non-allergic children and one-third were allergic children who were suffering from a major allergy. Of this group of 200 cases, none showed reactions to penicillin by the scratch test, three showed reactions by the intracutaneous tests and none of these patients were clinically sensitive to penicillin. In order to demonstrate that the test materials being used could produce positive reactions, these reactions were performed on several adults

on the hospital staff who were known to be clinically sensitive to penicillin and positive reactions were obtained in three of these. The authors conclude from this study that penicillin sensitivity reactions in children are very rare as compared to adults but that in allergic children, as shown by the incidence of 6 per cent in eighty-five private patients selected at random, the incidence is not low. They further conclude that skin testing has little value in the evaluation of penicillin sensitivity, but that a determination of penicillin sensitivity depends on the history of previous administration of the drug and any reactions which resulted. In this study, they also found no correlation between positive skin tests with penicillin and those with the penicillium molds.

ALLERGY TO DRUGS OTHER THAN PENICILLIN

Brown[9] reviews the subject of drug allergy in great detail, but the review will not be completely summarized here. The two chief values of the review are: (1) The author lists the clinical syndromes, such as urticaria, bronchospasm, dermatitis, et cetera, which can be caused by the use of drugs and under each of these clinical syndromes lists the drugs which have been known to cause these syndromes; (2) He includes a long list of drugs in alphabetical order listing the allergic reactions which have been reported due to them, and gives references in the literature for many of these. Both of these lists are easily available for ready reference for anyone who is interested in a particular clinical syndrome due to drug allergy, or in a particular drug and the effects which it may cause in the patient, other than those for which the drug is given.

Criep and Ribeiro[18] describe three fatalities due to allergy to procaine hydrochloride. They classify reactions in local anaesthetic drugs as: (1) toxic, and (2) allergic. They subdivide the allergic reactions: contact dermatitis, serum sickness type reactions, anaphylactic or accelerated serum sickness type reactions, and atopic reactions. In one of the cases reported, the individual was atopic and the injection of the drug produced an acute bronchospasm leading to asphyxia and death. In the other two cases reported, there was an immediate fatal anaphylactic reaction. The authors point out that skin testing is unreliable in this condition and that the best test with procaine hydrochloride is to apply the drug with an applicator intranasally and if the subject is seriously sensitive, untoward symptoms will develop within a few minutes. If the preliminary test is negative, it may be assumed that further administration of the drug is relatively safe. However, if there is a history which leads to a suspicion of sensitivity, a drug whose chemical structure is unrelated to procaine hydrochloride should be employed.

FOOD AND DIET MODIFICATIONS

Ratner et al,[64,65,66,67] in a series of four papers, discuss the allergenicity of modified and processed foodstuffs. In the first paper[64] the authors discuss the use of a dual ingestion passive transfer test to determine the allergenicity of foodstuffs in man. The method of this test is as follows: The donor, an allergic subject with a negative history for virus hepatitis and syphilis, has been tested to food allergens. Donors, skin sensitive to food proteins and clinically sensitive as well, are used. Serum is separated from the blood drawn from these patients and tested for sterility. It is then frozen or lyophilized and when reconstituted will be ready for use. Recipients are preferably non-allergic subjects who are skin tested to rule out hypersensitivity to the substance under investiga-

tion. Throughout the test period, all the foods to which the donor reacts must be completely eliminated from the recipient's diet. In the test, the donor's serum is injected into several sites of the recipient to produce passive sensitization as in the Prausnitz-Kustner passive transfer test. To determine whether the donor's serum contains specific circulating allergic antibodies to the foodstuffs under investigation, one of the passively sensitized sites is tested directly twenty-four to forty-eight hours later with the food protein to which the donor reacts. If a skin reaction ensues at the prepared site, the indication is that the donor's serum does contain circulating antibodies for specific foods. Twenty-four to forty-eight hours after the direct skin test the recipient ingests the modified processed foodstuff under investigation. If no reaction ensues in the passively sensitized areas, the recipient then ingests the food in its native form twenty-four to forty-eight hours later. The absence of reaction from the ingestion of food in modified form and the subsequent presence of a reaction following ingestion of the same food in native form objectively demonstrates that some change has occurred in the allergenicity of the foodstuff from the heat treatment or other processing to which it has been subjected or that it did not pass through the intestinal wall. The positive reaction usually occurs within fifteen to thirty minutes and persists for several hours. Preliminary experiments yielded the following results: egg protein subjected to moist heat appears to lose some allergenicity of the albumin and globulin fractions but the ovomucoid fraction is not entirely affected in this respect; hence, the individual sensitive only to the former fractions will be able to tolerate a hard boiled egg, whereas the individual sensitive to ovomucoid may not. Fish proteins appear to remain highly allergenic in spite of subjection to moist heat. Cod liver oil was shown to have no allergenicity in relation to codfish hypersensitivity. Peanut oil was found to be non-allergenic whereas peanuts are highly allergenic. Orange juice devoid of seed protein and peel oil is hypoallergenic and non-irritating. The authors feel that this method should be adopted specifically for the study of the allergenicity of foodstuffs and should supplant the doubtful trial feeding methods where conclusions are based on subjective rather than objective results.

In the second paper[65] they report the anaphylactogenic properties of a specially prepared infant orange juice determined in the guinea pig. To do this, they used a double shock technique; that is, in the procedure a second challenging dose of the material used for sensitization was given an hour or more after a negative reaction was obtained with the first challenging injection of the modified form of the substance under investigation. The purpose of this was to determine whether the animal was sensitive to the original material. In this study, anaphylactogenicity of the protein derived from orange seed was found to be of a high order but that due to the orange juice under study gave evidence of anaphylactogenicity only in a concentrated form, and it was shown that the orange juice did not contain orange seed protein in an amount detectable by the methods employed, and that the proteins in the seed and in the juice had independent antigenicities. The orange peel oil, on the other hand, was shown to be primarily toxic and not to have anaphylactogenic properties in the dilutions employed. The authors conclude, therefore, that the juice under investigation was devoid of seed protein and peel oil and, within the limits of the experiment, to be hypoallergenic and non-toxic.

In the third paper[66] they discuss the allergenicity of peanut and of peanut oil using the dual ingestion passive transfer test and also anaphylactic

tests in the guinea pig. By means of the former test, it was demonstrated that peanut oil, taken in large amounts, failed to elicit reactions at the sites in the subjects passively sensitized with the peanut antibody, but that the ingestion of the whole ground peanut gave positive reaction in sensitized sites of all the individuals who gave negative reactions to the oil. In the same manner, it was demonstrated that Bremil, an infant food containing peanut oil, taken in the amount usually ingested in an average instance, failed to elicit reactions in the sensitized skin sites. By the use of the passive transfer tests with this same serum, it was demonstrated that penicillin in peanut oil did not contain enough peanut antigen to elicit allergic reactions in the children who received the penicillin by injection. By the anaphylactic experiments on guinea pigs, it was demonstrated that both the refined peanut oil and Bremil are non-anaphylactogenic. Peanut oil, therefore, can be ingested or injected into peanut allergic individuals. This paper demonstrates a method of settling the controversy which arises as to the allergenicity of purified oils such as cod liver oil, peanut oil and cottonseed oil, which is present in oleomargarine. Most of the experiments which have been done in the past have consisted essentially of ingestion experiments where the results depend on subjective symptoms of the recipient. In the method described in these papers, all conclusions are based on objective findings and therefore are not open to question of interpretation as they are in feeding experiments.

The fourth paper,[67] on the allergenicity of orange in man, made use of both the Prausnitz-Kustner method and the dual ingestion passive transfer test in children. These tests were done both on children who were not known to be allergic to orange and those who were known to be allergic to orange. By these experiments, they showed that orange juice protein does not appear to traverse the gastrointestinal wall readily, even ingested in large amounts, and that only in rare instances does true orange allergy produce such clinical manifestations as urticaria, asthma or eczema. In these instances, the symptoms seem to be largely or entirely due to orange seed protein. Although orange seed protein does not readily traverse the wall of the gastrointestinal tract, it was demonstrated to produce allergic reactions when injected parenterally into passively sensitized sites. Orange peel oil, on the other hand, possesses toxic and irritative properties but is non-allergenic. The authors feel that local dermatitis and gastrointestinal symptoms generally attributed to allergy to orange, are not always allergic in character but rather psuedo-allergic dermal and gastrointestinal irritation produced by the primarily toxic orange peel oil. Bib orange juice, the only product tested, is devoid of seed protein and orange peel oil and is therefore free from allergenic properties found in seed protein and from the non-allergenic irritant found in peel oil, and therefore can safely be ingested by patients who are allergic to the seed protein. These two papers on orange sensitivity put a different aspect on what we usually refer to as allergy to orange juice, demonstrating that there is little or no allergy to orange juice protein itself but rather that the allergy is due largely to any protein of the orange seed which may be present in the juice. This has very obvious implications in the feeding of allergic infants.

Johnstone and Glaser[40] describe the use of soy bean milk as an aid in prophylaxis of allergic disease in children and they do this by substituting soy bean milk for cow's milk from birth until the age of six to nine months in all cases under study. The experimental group was made up of ninety-one infants who were either offsprings or siblings of one or more individuals with one or more major allergies. These infants were

fed soy bean formula instead of cow's milk. The histories of sixty-five siblings of those in the experimental group served as a control group and a second control group was made up of 175 unrelated children with approximately the same allergic family history. From each group the following data were sought: (1) The total incidence of major allergic diseases; (2) The incidence of atopic dermatitis; (3) The incidence of other allergies to cow's milk such as colic or diarrrhea; and (4) The allergic sequellae of atopic dermatitis and other allergies due to cow's milk. It was found that major allergic disease developed in 14 per cent of the experimental group, in 64 per cent of the siblings and in 52 per cent of the unrelated control group. Atopic dermatitis and other expressions of allergy to cow's milk occurred approximately four times more frequently in the two control groups. These observations were all statistically significant and the authors therefore feel that the complete withholding of the first food commonly ingested by a potentially allergic newborn infant, that is, cow's milk, for a period of six to nine months, may offer a hope of decreasing or minimizing the incidence of the most troublesome allergic disorders in young children.

Glaser[33] reviews the history of substitutes for cow's milk in infant feeding, discussing soy bean milk; nutramigen; goat's milk; mare's milk; ass's milk; reindeer, llama, wild buffalo, and camel's milk; the milk of the anthropoid ape; milk substitutes made from nuts; cereals and taro; and milk substitutes made from strained meats, beef, lamb, pork and whales. He gives the formula for cow's milk substitute containing strained meats.

GASTROINTESTINAL ALLERGY

Withers[92] presented a masterful review of gastrointestinal allergy, including pediatrics, from its inception to the present.

Rothman[71] reviews the recent literature on diarrhea of allergic origin, but this review will not be completely detailed here. Initially, he discusses gastrointestinal allergy in general with emphasis on some of the more important previous work in this field and the difficulties in diagnosis. He then reviews the literature on diarrhea of allergic origin, the discussion being limited chiefly to infants under two years of age. He discusses two clinical groups in this age group: (1) severe diarrhea during the neonatal period with rapid loss of fluid and electrolytes, and (2) chronic diarrhea during the second year of life simulating cases of celiac disease.

Kunstadter and Schultz[43] report several cases of gastrointestinal allergy, many of which exhibited the celiac syndrome, and refer particularly to allergy to cow's milk. They quote several authors who have pointed out that the celiac syndrome is sometimes due to food allergy and from their own experience agree that cow's milk is the most frequently encountered allergen responsible for allergic diarrhea. They report thirty-six cases of chronic, recurrent diarrhea, eleven cases clinically presented the celiac syndrome, and cow's milk was the principal offending allergen in all. In almost half of the thirty-six cases studied, gastrointestinal symptoms, particularly diarrhea, began during the first three months of life and of the eleven cases of celiac syndrome, four began during the first three months of life. Fifty per cent of the thirty-six cases had a history of some form of allergy in the immediate family, parents or siblings, and 50 per cent had some manifestation of allergy other than diarrhea, such as eczema or asthma. Seventy-three per cent of those with the celiac syndrome gave a family history of allergy and showed other manifestations of allergy. Many of the infants were able to consume cow's milk without diarrhea after

abstinence for periods of three to forty-two months, an average of 18.3 months, usually at the age of two and one-half to three years. Of the eleven cases of the celiac syndrome, eight required elimination of cow's milk from eleven to forty-two months, an average of 21.4 months. They were able to tolerate cow's milk without recurrence of the celiac syndrome at an average age of three years. The authors feel that, from a diagnostic standpoint, the allergic history is of extreme importance since so many of these cases have a history of allergy in themselves or in their immediate families. They feel further that a diagnosis of gastrointestinal allergy due to cow's milk is fairly easy to make because the gastrointestinal symptoms completely disappear on eliminating cow's milk and all dairy products from their diet, often within two days, frequently within several days, and a prompt recurrence of these symptoms appears when these foods are reintroduced into the diet. It has been their experience that after a period of several months, when the infant has reached a good stage of nutrition with consistently normal stools, re-introduction of cow's milk may be attempted in small amounts gradually increasing to tolerance. They do not feel that skin tests are helpful as a diagnostic procedure in gastrointestinal allergy.

This is an extremely important paper, not only because it draws attention again to the importance of considering gastrointestinal allergy as one of the etiologies of the celiac syndrome, but also because it draws attention to gastrointestinal allergy in infants in general. While it is difficult to give any good appraisal of the incidence of gastrointestinal allergy as a cause of such difficult-to-treat syndromes in infants as colic, irritability, diarrhea, vomiting, flatulence and regurgitation, it would appear that many of these cases are due to gastrointestinal allergy and it is very important for the pediatrician and allergist to recognize these and treat them properly. Certainly, it would seem reasonable, in any of these cases which do not respond to the usual methods of treatment, such as anti-spasmodics or sedation, to give the infants a trial of an elimination diet, first of all eliminating cow's milk and dairy products and secondly eliminating wheat and other foods which may be important in gastrointestinal allergy.

Squier[81] discusses the problem of gastrointestinal disturbances attributed to allergy. He points out that when acute gastrointestinal symptoms are caused by an allergic reaction, the causal relation usually is recognized readily, but there is widely divergent opinion concerning the rôle of allergy as a cause of chronic indigestion, diarrhea and a multitude of other nondescript digestive symptoms and complaints. Rowe, on the one hand, feels that a large percentage of all symptoms arising in the alimentary tract are due to food sensitization. Cooke feels that this is unusual. The author records the incidence of symptoms that might be attributed to gastrointestinal allergy in the last 1000 consecutive private patients seen. Since all of these patients had been considered allergic, one might justifiably expect gastrointestinal allergy to be encountered more frequently than in a group less weighted by allergy. However, it was found that of the 1000 patients, chronic gastrointestinal symptoms were recorded in only twenty-eight patients and a diagnosis of gastrointestinal allergy was believed justified in only seven of these. However, some other patients did report past acute gastrointestinal allergic reactions to certain foods in their histories. In the series, there were only two patients who had chronic ulcerative colitis and in neither of these was allergy considered of etiologic significance, nor was sensitivity to foods found. The author does not feel that roentgen studies are of much importance in the diagnosis of gastrointestinal allergy. He uses a modified provocative diet to identify or exclude major food

allergens and later forced trial feedings and withdrawal of suspected foods aid in recognition and identification of these foods clinically responsible for symptoms. A symptom-free period during trial elimination of a suspected food is suggestive but is not sufficient evidence alone to justify the diagnosis of hypersensitivity. In addition, symptoms must be reproducible at will when suspected foods are included in the diet. This study includes quite a large number of children, but most of the patients studied were adults. The author well places emphasis on the fact that all gastrointestinal symptoms, especially of a chronic nature, must not be concluded as being due to allergy and that the diagnosis of gastrointestinal allergy whether to foods or other allergens, rests a great deal on history, elimination of the suspected allergens and the return of symptoms when the allergen is again given to the patient.

IMMUNOLOGY

Menzel et al[51] report further studies on the location of the skin sensitizing antibody in certain fractions of ragweed reacting sera. Their method is to separate the plasma fractions electrophoretically from ragweed sensitive patients in whom circulating antibodies have been demonstrated, and then do passive transfer tests expressing the end point of reactivity, not in terms of dilution, but in terms of the actual amount of protein component injected into the skin site. The sites were prepared by the injection of ragweed-reacting sera or their fraction and the sites tested in the usual manner. This study, and previous studies on the same subject, show a variation in sera from different ragweed sensitive patients as to the location of the sensitizing antibody in the alpha 2, beta and gamma globulin fractions or in the interzones of these components. However, neither gamma globulin, beta globulin nor alpha 2 is essential to skin reactivity since reactions have also been found in the absence of each of these components in electrophoretically detectable amounts.

Vaughan et al[90] studied the reagen content of the plasma proteins of four patients with ragweed hay fever, fractionated by Cohn's alcohol precipitation method. They found the skin sensitizing antibody of ragweed hay fever to be concentrated among the proteins of fraction 3D as separated by alcohol precipitation in the cold. This fraction consists primarily of the beta globulins.

Malkiel and Feinberg[46] carried out neutralizing antibody titrations in a series of non atopic human volunteers receiving one of eight ragweed preparations. A total of over 370,000 protein nitrogen units of ragweed extract was administered during the course of twenty-six weekly injections, but no significant increase in neutralizing antibody was detected after such a series of injections. The neutralizing antibody titrations were done according to the technique of Loveless with certain minor modifications.

These three papers demonstrate that a great deal is still to be learned about the actual immunology of the allergic patient, why certain individuals are much more allergic than others, and why the hyposensitizing injections which we give are effective. This field of investigation is certainly one of the most essential for the proper understanding and treatment of the allergic patient.

PSYCHOSOMATIC ALLERGY

Abramson[2] in a review of a psychosomatic allergy and its management, first of all reviews the literature on this subject for approximately the past five years and demonstrates that irrespective of what antigen-anti-

body mechanism may account for the syndrome of hypersensitivity, the management of the patient with allergy requires consideration of total family constellation and must involve psychosomatic studies as well as skin testing, et cetera. In the second part of the paper, he reports a verbatim recording showing how a conflict situation led to itching and scratching, independent of known antigen-antibody sensitivities in a patient, and uses this to demonstrate the use of verbatim recordings both in psychotherapy and in psychoanalytic procedure. He concludes that it is the function of the allergist to manage the patient as a whole and to embody in the management the integration of mind-body functions of the patient.

Rosenthal[70] presents a psychosomatic study of infantile eczema and the thesis of his paper is that eczema arises in certain predisposed infants because they fail to obtain from their mother or mother's substitute adequate soothing physical contact. The author made a study of twenty-five infants under two years of age who had eczema, and eighteen controls of the same age group without eczema. He studied them from the point of view of the amount of physical contact which existed between the mother and the child and found that in a significantly higher proportion among the eczema cases, the mother tended to let the baby cry without picking it up unless some obvious physical discomfort was present and concludes that most eczematous infants receive inadequate caressing and cuddling. He feels, in fact, that this is the most important etiologic factor in eczema but admits that other factors such as constitutional predisposition and allergy are possibly equally important. He stresses the fact that he realizes his study considers largely the quantity of physical contact and does not give much emphasis to the quality of the physical contact. Anyone who has seen and treated a great many cases of eczema in infants will admit that it is a very complex problem and cannot always easily be explained entirely on antigen-antibody relationships inasmuch as exacerbations, which cannot be explained on any difference in food, inhalants or physical factors, do occur. However, in a great many cases, it is possible to find etiologic factors such as wheat, milk and egg and by removing them and instituting local treatment, a complete clearing of the rash occurs quite independent of any change in the mother's attitude towards the child. Similarly, there are many cases where eczema develops in a child which has a normal, happy relationship with his mother, and who is given adequate physical contact with the mother. Therefore, it is very difficult to see how the thesis of the author that handling of the child, or lack of it, is the most important consideration in the etiology.

Miller and Baruch[52] describe techniques for handling the acute attack of bronchial asthma from a psychotherapeutic point of view. The method consists essentially of approaching the attack of asthma by feeding the affect hunger, by lessening the fear of rejection and when possible, by lessening the patient's anxiety over his hostile components and helping him to release them. These techniques apply both to children and adults.

MISCELLANEOUS

Two papers have appeared on the general management of the allergic child. Stevenson[83] stresses that an allergic child is a well child with a life-long problem and that in his care it is essential to treat the whole child and not simply treat his allergy without any attention at all to his emotional development which can easily be distorted by the constant therapy. The author's point is well taken that the treatment of an allergic child should include the care of the whole child and for this

reason, it is much better for an allergic child to be under the care of a pediatric allergist.

Criep[17] in a general discussion of allergy in children, including recognition of the allergic nature of the presenting condition, establishment of an allergic etiology and the institution of allergic treatment, discusses respiratory, dermal and gastrointestinal allergy.

Chobot[13] stresses the importance of infection, particularly foci of infection, in both childhood and adult allergy as important in the etiology and treatment of both dermal and respiratory allergies. He points out that the importance of an infection in these allergies can be demonstrated by the therapeutic results seen after removal of foci of infection and by exacerbation of the disease following the injection of autogenous vaccine. The foci in children are most frequent in tonsils and adenoids. Skin tests with bacteria are useless. He feels that in asthmatic children, infection is the most important single cause of the disease, but stresses that other forms of allergy, namely, inhalants and foods, must also be considered in a therapeutic regime. Many allergists would disagree with this, feeling that inhalants are more important in the etiology of the allergic condition than bacterial allergy. However, all would agree that bacterial allergy pays an important rôle in many cases and that foci of infection should definitely be removed.

Fries and Borne[32] discuss remission of intractable allergic symptoms by acute intercurrent infections. They report thirty-two atopic children who while under observation showed a temporary remission of their allergic symptoms following a viral or bacterial infection. These children were suffering from asthma, perennial rhinitis or eczema. Eleven of the subpects had measles, two pneumonia, one scarlet fever, two upper respiratory infections with sore throats; the other sixteen suffered with Kaposi's varicelliform eruption. In several instances, modification of the allergic status was dramatic and in some the remission period was sufficiently long for the patient or the parents to think that a complete recovery had been effected. Some remissions lasted up to twelve months. The authors also review the literature on this subject, describing remissions which have been reported following such various illnesses and operations as penumonia, tonsillectomy, appendectomy, jaundice, either infectious hepatitis or serum hepatitis, pertussis, varicella, mumps and roseola. They feel that measles is the most outstanding and consistent in its modification of the allergic process. However, they point out that there is no constancy of beneficial effect of these diseases on the allergic state and that very frequently an adverse effect is seen. While it has been observed repeatedly that virus infections produce a very temporary remission of allergic disease, it is certainly the consensus of opinion that bacterial infections such as pneumonia or tonsillitis make the disease worse during the course of the acute illness. However, as these authors have shown, there are definite exceptions to this. One must be very cautious, however, in interpreting these prolonged remissions of a year or longer as being due to the acute illness, because we all know that these remissions of a very prolonged and even permanent character occur in all of the acute allergic diseases without any intercurrent infection, operation or other possible causative agent being found.

Editorial, *The Journal of Pediatrics*[23] points out that one of the chief difficulties in establishing a definite relationship between a bacterial infection and symptoms of an allergic nature lies in the failure of bacterial extracts or vaccines to produce the characteristic and immediate whealing

types of skin reactions which are so useful in the diagnosis of allergic conditions such as hay fever to pollens, et cetera. The problem of bacterial allergy involves allergic sensitization to bacterial products; in other words, the nucleoprotein and/or an endotoxin of the organism concerned. In spite of the controversy regarding the rôle of bacteria in allergy, there are good reasons, as has been pointed out by Cooke, for the theory that bacteria themselves or their products may cause allergic reactions. (1) A familial background of allergy is particularly common in acute infectious asthma of infancy and early childhood. (2) The significant association of asthma due to infection with asthma due to inhalants, drugs, or foods or with other accepted allergies, such as hay fever and eczema. (3) Eosinophilia is often present in asthma where infection appears to be the sole etiologic factor. (4) The asthmatic attack can sometimes be reproduced by very small doses of bacterial vaccine. However, only by careful allergic investigation and then only from a clinical viewpoint, can one arrive at a diagnosis of bacterial allergy.

Two papers have appeared on the subject of the rôle of immunization procedures in the precipitation of poliomyelitis. Rhodes[68] reviews the published evidence on the association between poliomyelitis and immunizing injections and analyzes the inoculation histories of cases of poliomyelitis which occurred in Canada in 1951. He also discusses 235 cases of paralytic poliomyelitis which were investigated at the Hospital for Sick Children in Toronto, and from these analyses, concludes that there is no reason to recommend that immunization be suspended in Canada during the poliomyelitis season.

Abramson[1] reports an attack on this problem from the other direction, namely, an attempt to determine the influence of injections of specific antigens employed in the therapy of pollen hay fever and asthma as they might influence the poliomyelitis syndrome. This report is the result of a survey, which was undertaken by a questionnaire sent to allergists throughout the United States asking the number of patients that they had taken care of during the summer who had received pollen injection therapy and the number of infantile paralysis cases which had been observed in this group. Over 800 allergists responded with data covering 153,749 patients. Only twenty-nine cases of poliomyelitis were reported in this group of patients which was the approximate anticipated rate. Thus, immunization by pollen extracts was concluded not to increase the incidence of infantile paralysis and the type of immunization as indicated by the small series did not increase bulbar paralysis or affect the location of the paralysis when it occurred.

These papers and papers on the same subject which have appeared in the past should settle once and for all the controversy about the effect of immunizing injections on the production of poliomyelitis.

Segal et al[76] describe in detail the syndrome of respiratory acidosis and give a very complete description of the syndrome of so-called carbon dioxide intoxication. First of all, they summarize the manifestations of respiratory acidosis pointing out that the symptoms may be mild with weakness, headache, lassitude, irritability, personality and mood changes, or they may be severe with confusion, stupor, coma and eventually death. They then discuss the normal control of respiration and the normal acid-base balance. They list the various steps in the pathogenesis of respiratory acidosis and the factors involved in the etiology of respiratory acidosis. Next they describe the diagnosis of respiratory acidosis and then the treatment, emphasizing that one should avoid high concentrations of oxygen

and also avoid respiratory depressing drugs. When oxygen must be given to a chronically hypoxic patient, it should be administered in a graded program, starting with low concentrations and increasing gradually every one or two days. Sedatives and narcotics should be used with caution. It is very important to maintain and restore effective alveolar ventilation. Editorially, in ANNALS OF ALLERGY[25] Segal's paper is discussed and it is pointed out that this syndrome of respiratory acidosis is not usually encountered in the course of the acute attack of bronchial asthma or in status asthmaticus unless the patient has underlying chronic pulmonary disease.

Two papers have appeared on undesirable effects obtained by the use of antihistaminic drugs. The first by Judge and Dumars[41] describes intoxication with benadryl and pyribenzamine in children. They state that with these drugs, half of thirty cases of severe intoxication that have been reported have been in infants and children. The two primary effects on the central nervous system are first of all stimulatory effects, and then depressive effects. Children are more susceptible to the stimulatory effects of these drugs. The effects on the central nervous system involve both the cerebrum and cerebellum with initial stimulation followed terminally by depression. They list in table form the effects under headings: central effects; depressive effects; neuropsychiatric effects; peripheral effects, and effects on the special senses. They report two cases of severe toxicity to these drugs, one in a two-and-one-half-year-old child and the other in a two-year-old child. Both of these children were poisoned accidentally. They then discuss treatment of poisoning due to these drugs, pointing out that there is no specific antidote but that treatment must be purely symptomatic: evacuation of the stomach, sedatives for evidence of stimulation, and stimulants for evidence of depression. They emphasize that the child must be very closely watched by a physician because the picture changes rapidly and the treatment has to be changed accordingly. While it is true that the antihistaminic drugs have been used much too widely, particularly for such conditions as common cold and also in allergic conditions as a replacement for proper anti-allergic treatment, these reports of poison do not condemn the drugs in themselves because there are many cases of poisoning due to commonly used drugs such as aminophylline which all allergists use a great deal. However, the article does serve as a warning not only against the indiscriminate use of antihistaminic drugs but against leaving any drugs where they can be obtained by children and so cause accidental poisoning.

In the second paper, Schaffer[72] analyzes the effect of certain antihistaminic drugs given to twenty-three children for various allergic states over a period of from one month to two years. Before therapy was started, all these children had been well adjusted. After the start of antihistaminic therapy, all of these children developed personality changes with crying, irritability, disobedience, anorexia, weeping and antagonistic or obstinate tendencies. The medical examination in each case revealed an apprehensive or antagonistic child. The antihistaminic drugs were being employed only in the recommended doses. In all cases, the symptoms disappeared within one or two or three days after the offending drugs were stopped. In those cases where the antihistamine had been given along with ephedrine or aminophylline, these drugs were given separately without producing similar personality changes but when the designated antihistamines were again prescribed, the behaviour symptoms reappeared.

Ratner[60] discusses bone maturation and capillary microscopy as in-

dicators for the use of thyroid in childhood allergy. He feels that every allergic child must be treated from every point of view. Some of these children show thyroid hypofunction, and unless this basic constitutional deficiency is corrected, other modes of therapy may be only partially effective. The usual methods for determining thyroid hypofunction are impractical for office procedure but he feels that bone maturation and capillary microscopy are helpful in making this diagnosis. Bone maturation is easily determined by fluoroscopic and roentgenographic examination of the bones of the wrists and the hands and films should be repeated yearly. There is not yet sufficient evidence that the chronic allergic state *per se* causes deficiency in the skeletal development and this deficiency is often due to hypothyroidism. Hypothyroidism in the allergic child does not occur more frequently than in children of the general population. The presence of several of the signs of hypothyroidism, coupled with bone retardation, add up to a definite syndrome often referred to as masked hypothyroidism, a mild form of thyroid deficiency. The method of doing capillary microscopy is next described and the history of this study briefly discussed. This also is another method of establishing thyroid deficiency. Thyroid therapy is usually started with grains ¼ in the younger age group and grains ½ in the older child. The patient is checked regularly and the dosage gradually increased until the desired effects are obtained in better health and gain in weight. Seldom is it necessary to use more than 2 grains of dessicated thyroid daily. The best results are obtained in the eczematous patient and in certain cases of infantile eczema the response is quite dramatic. In respiratory allergies, thyroid apparently aids in reducing mucosal edema in the respiratory tract, but the author does not believe that the therapy relieves the true allergic attacks of asthma, nor does it lessen the frequency of such attacks. The author concludes that in the treatment of the allergic child, the response to thyroid therapy is a rewarding experience.

O'Rourke et al[54] describe the reactions to the bite of a mosquito on thirty-six volunteers who were bitten at two sites, one of which was treated with an antihistaminic cream, 2 per cent pyribenzamine, and the other left untreated. The severity of the reaction was diminished in 60 per cent of cases. An anesthetic cream, 1 per cent nupercaine, was found to be 80 per cent effective in relieving the pruritus as was the pyribenzamine but as the antihistaminic was also effective in reducing the severity of the lesions, it was considered slightly superior to the local anesthetic.

Parish[56] reports on the oral administration of procaine hydrochloride with ascorbic acid in allergic patients who were complaining of pruritus. He reports thirty-one cases, many of whom were children. The drug produced relief in twelve of thirteen cases of atopic dermatitis, eight out of nine cases with contact dermatitis, three out of four with poison ivy, and also in some miscellaneous conditions. He concludes that the use of this combination offers a new and effective method for the treatment of pruritus. In some cases, dramatic relief was reported within minutes and in most cases, relief continued from four to six hours. No toxic effects were observed.

Sheldon et al[78] discuss skin testing techniques and the reliability of the skin tests in atopic disease. They conclude that skin tests are a valuable procedure when properly interpreted in the light of clinical history, that tests done with inhalants are highly reliable, but that tests done with foods are often not reliable but sometimes of value.

Criep et al[19] studied the effect of cortisone on several aspects of

experimental hypersensitivity. They used rabbits for the purpose of demonstrating precipitin titers, the Arthus phenomenon, diffuse arteritis and the Schultz-Dale phenomenon, and guinea pigs for the purpose of demonstrating anaphylaxis and the Schultz-Dale phenomenon. They found that cortisone does not affect the precipitin titer if administered during, or prior to and during, sensitization. The Arthus phenomenon, anaphylactic shock, and the Schultz-Dale reaction in the isolated ileum strip performed in the manner described also remained unaffected. Cortisone tends to inhibit experimental diffuse vascular reactions. In addition, they demonstrated that anaphylactic shock and the Arthus phenomenon were unaffected by the administration of compound F.

Swinny[86] reviews twenty-five cases of allergic parotitis that have been reported in the literature and adds one case, that of a thirty-one-year-old woman who had suffered from recurrent swellings of the parotid gland for nine years. She also suffered from hay fever. The fluid obtained from the parotid duct on the side of the swollen gland was thick, jelly-like and contained 100 per cent eosinophiles. She gave positive skin tests with many pollens and several foods, including wheat, and by elimination diets wheat was found to be the etiologic agent, the parotid swelling could be produced at will by the ingestion of wheat. The author describes the pattern of allergic parotitis as: (1) usually a personal and/or family background of allergy; (2) recurrent attacks of unilateral or bilateral swelling of the parotids; (3) thick, ropy saliva that often forms plugs or casts of the ducts; (4) sputum contains many eosinophiles; (5) the attacks are precipitated by specific allergens, inhalants or ingestants and are relieved and prevented by avoidance or hyposensitization.

Ratner et al[62] published in abstract form, a symposium presented at the 1952 Annual Meeting of the American Academy of Pediatrics on the basic mechanisms in allergic disease. Four subjects are covered: (1) recent developments in the cellular transfer of hypersensitivity and antibody formation; (2) the pathology of the allergic and collagen diseases; (3) physiologic mechanisms of anaphylaxis and allergy; (4) some of the mechanisms by which drugs and antibiotics produce reactions.

Ratner and Silberman[63] have published a critical analysis of the hereditary concept of allergy. They point out that the discrepancies noted in published observations on the distribution of allergy, its relation to heredity, and the inferences drawn therefrom are largely due to different methods of collection of data, the criteria employed in defining the allergic state and the extent to which inquiry was made into the individual family incidence of allergy. For example, in a study which they did in 250 allergic children and their families, they found that if they inquired into the direct antecedents of the patient and the collateral antecedents, they found an incidence of allergy of 54.4 per cent in the family. If they inquired only as to the parents and grandparents an incidence of 43.2 per cent and if they inquired as to the parents an incidence of only 22.4 per cent. Because of this discrepancy, there is considerable variation in the published reports showing that allergy is an inherited disease. They feel that the commonly accepted belief that allergy is inherited is based on a few striking family pedigrees which have been reported in the literature. In the 250 patients and their families which they studied, there were 6,244 individuals and in these the incidence of allergy was only 9.8 per cent which agrees very well with the general agreed incidence of major allergic syndromes in the random population which varies from 7 to 10 per cent. They then discuss a monograph published by Schwartz[74]

in which he studied the problem of inheritance of bronchial asthma. Schwartz concluded that bronchial asthma is a genetic entity and that a genetic relationship exists between asthma, vasomotor rhinitis and probably infantile eczema, in which the specific offending allergen is clearly demonstrable. However, they do not feel that Schwartz proved his point that asthma is an inherited disease, and they conclude that in view of the conflicting conclusions that have been drawn by different investigators in an attempt to apply Mendelian laws to allergy, difficulty in obtaining adequate material, and inadequate definition of essential criteria, no genetic hypothesis can be made to fit the existing data.

Piraino[58] describes one case of Schonlein-Henoch syndrome in a three-year-old child who had a typical clinical picture. The onset followed the administration of penicillin. The child was put on a strict elimination diet and it was found that egg gave some symptoms. However, the patient had received penicillin on two occasions previously, the first time with no symptoms and the second time having been followed by vomiting and abdominal cramps. The author concludes that penicillin was the main allergen causing the allergic response in the child although egg sensitivity probably played a secondary rôle. The history and clinical picture of the disease are also discussed.

Bowen[7] reports fifty-nine pairs of identical twins all of whom were confirmed as being monoplacental. The youngest pair was eight weeks old and the oldest pair fifty-six years old, but the majority were between six and fifteen years of age. Of the fifty-nine sets, only seven sets presented dual allergies while the remaining fifty-two pairs had allergy of a sufficient degree for one of them to seek medical help in only one of each pair of twins. This is contrary to the usually accepted observation that identical twins tend to have identical allergies. The author points out that these results are in contradistinction to the concept that allergic manifestations are the result of placental transference, as one would expect all fifty-nine sets of twins to show bilateral allergy and also that it challenges the concept that by making maternal dietary restrictions during pregnancy, allergy is less likely to appear in the newborn. This study is very interesting inasmuch as most of us tend to think of identical twins as having identical illnesses and allergies, whereas these patients were all carefully studied and the reverse was found to be true. On the other hand, it is not against the concept of allergic manifestations being the result of placental transference for even the strongest proponents of this concept do not claim that all allergy is derived in this way. For this reason, it is not necessary to postulate that one affected twin became allergic because of placental transference whereas the unaffected twin did not suffer the same transference. Similarly, the study does not challenge the concept of making maternal dietary restrictions during pregnancy because here again, the strongest proponents do not claim that this will prevent all allergy. They merely point out that it will minimize the chances of allergy developing, something which is, in no way, contradicted by this study on twins.

Devanney and Shea[21] report a case of allergic encephalopathy with papilledema and point out that allergy must be considered in the differential diagnosis of the vague group of disturbances classified as pseudo-tumor or encephalopathy of undetermined cause. They report one case of a nine-year-old boy who had hay fever due to pollens and who was sensitive to certain foods. At three and one-half years before admission, he had an episode of headache, lethargy, double vision and papilledema which

cleared spontaneously. The attack had come on following a visit to the zoo. At nine years of age, when he was studying, he again complained of headache and had papilledema of two or three diopters. Ordinary neurologic investigation including air encephalogram was negative but he gave positive skin tests with foods, pollens and molds and the performance of the tests was associated with a marked increase in the headache and lethargy. He was treated with elimination of the positively reacting foods, hyposensitization to the pollens and molds and with antihistaminics. There was a remarkable relief of headache within the first twelve hours following the administration of the antihistaminics and the child recovered with no recurrences. The authors point out that this is not a definitely proven case of allergic encephalopathy but that it would appear from the investigations that this was the etiology of the disease.

Larkin[44] reports the seventh case of favism in a child in the United States. This is a one-year-old child who suffered the illness following the ingestion of fava beans. He points out that this is an allergic disease which can be suffered either following the ingestion of fava beans or the inhalation of the pollen if a susceptible person walks through or alongside a field of fava beans during the pollinating season. Most cases occur in childhood and adolescence although nursing infants are not immune if the nursing mother or wet nurse happens to include fava beans in her diet. Diagnosis usually depends on a history of contact with the bean or pollen. Skin tests or passive transfer tests may be negative for some weeks after an attack, but positive skin tests and passive transfer tests by the Prauznitz-Kustner technique have been demonstrated in some patients.

Three reviews of interest to the pediatric allergist have appeared during the past year. One by Halpin[35] is a review of miscellaneous allergy in the year 1952. The second by Collins-Williams and Ratner[15] is a review similar to the present one for the year previous to this year. The third by Fontana[30] is a review of some of the main articles published in the field of pediatric allergy during the past five years.

Two new allergy textbooks have appeared in the past year. Hansel[37] has written a new volume on clinical allergy. This book contains fiftv-three chapters covering the whole field of allergy, including five chapters on pediatric allergy. It is an excellent, comprehensive book on the subject of allergy. The second by Sheldon, Lovell and Mathews[77] is a very practical discussion of allergy, written from the viewpoint of a practicing allergist with only minimal emphasis on the theoretical aspects of allergy. Although it covers the major part of the field of allergy, it emphasizes practical procedures such as skin testing, other laboratory procedures, hyposensitization, symptomatic therapy, pollen identification, fungus and mold identification, sources of the various inhalant allergens, the office management of the allergic patient and the preparation of allergenic extracts for testing and treatment. It is an extremely valuable book for the practicing allergist and very useful for medical students and practicing physicians who are interested in the field of allergy.

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1421 Danforth Ave. (Dr. Collins-Williams)

News Items

THE ISRAEL SOCIETY OF ALLERGY

Since its foundation in 1949, the Israel Society of Allergy has been mainly a Jerusalem society. Single members from all parts of the country subsequently joined the society, which has consequently led to the establishment of groups in the major towns of Israel.

In Tel-Aviv, the group is headed by Prof. A. Klopstock and Dr. N. Lass; the Haifa group by Dr. R. Reitler and Dr. H. Seligman.

Interest in allergy has arisen in all parts of the country. Not only have lectures held in small towns been well attended, but the active participation of members of the audience in discussions has revealed that the country is gradually becoming "allergy minded." It is a matter of pride that the Jerusalem Society of Allergy has now become the Israel Society of Allergy.

To achieve larger audiences at the lectures, meetings have been held with other medical groups. This not only suits the place allergy takes in medicine between the medical disciplines, but makes it easier to find appropriate lecturers, whose number in such a small country as Israel must necessarily be limited.

In February, 1953, Dr. Leon Unger, of Chicago, delivered several lectures and participated in conferences of local chest physicians giving great impetus to the work of the allergists. It is hoped that his visit to Israel may stimulate other physicians to follow his example. It is suggested that the International Association of Allergology, of which the Israel Society has been a member since its foundation in 1951, should consider doing something constructive in this direction and persuade lecturers to come to Israel.

Meetings—1952 and 1953

1. January 20, 1952 (Jerusalem)—M. J. Gutmann: Second report on First International Congress of Allergy, Zurich, September, 1951.
2. January 27, 1952 (Tel-Aviv)—N. Lass and M. J. Gutmann: Constitutional meeting of the Tel-Aviv Group. Report on the Congress in Zurich.
3. February 19, 1952 (with Medical Organization, Jerusalem)—M. J. Gutmann: "Constitution and Heredity in Allergic Diseases."
4. May 16, 1952 (Haifa)—M. J. Gutmann: "Why Allergy Societies?" Foundation of the Haifa Group.
5. October 28, 1952 (with Medical Organization, Jerusalem)—Prof. A. Dostrowski: "Investigations Concerning Immunity and Allergy in Cutaneous Leishmaniasis."
6. February 16, 1953 (with Medical Organization, Hebrew University Medical School, and Hadassah Medical Organization, Jerusalem)—Leon Unger (Chicago): "Diagnosis and Differential Diagnosis in Bronchial Asthma."
7. March 3, 1953 (Tel-Aviv)—N. Lass: "Influence of ACTH and Cortisone on Biological Processes." W. Alkan: "Clinical Aspects of ACTH and Bronchial Asthma."
8. March 16, 1953 (Haifa)—M. J. Gutmann: "Contribution of the Studies of Adrenal Glands and ACTH for the Knowledge and Therapy of Allergic Phenomena."
9. April 28, 1953 (Jerusalem)—General Assembly. Election of a new committee, consisting of: M. J. Gutmann, G. Wintenberg, F. Sulmann and J. Tass.
   J. Tass: "Allergic Skin Reactions after the Use of Antibiotics."
10. August 18, 1953 (with Medical Organization, Jerusalem)—A. M. Cohen: "The Eosinophil Problem."
11. November 2, 1953 (Safad, Upper Galilee)—M. J. Gutmann: Questions and Answers on Allergy Problems.
12. December 21, 1953 (with Dental Association, Jerusalem)—M. J. Gutmann: "Allergy of the Oral Cavity; the Influence of the Teeth on Cold Allergy."
13. December 30, 1953 (Rishon le Zion)—M. J. Gutmann: "The Pollenallergic Diseases."

NEWS ITEMS

GERMAN SOCIETY FOR RESEARCH ON ALLERGIES—FOURTH CONVENTION

Extracts from the Program

Tuesday, April 27, 1954

President: Prof. Dr. Kikuth, Dusseldorf
Secretary: Prof. Dr. Hansen, Lubeck

1. The significance of the allergic pathogenesis in the case of arteritis (Free discussion.)
2. Secondary effects of modern medication therapy under special consideration of allergic reactions

Wednesday, April 28, 1954

1. Experimental allergic arteritis
2. About the periarteritis nodosa zosterica
3. Recidividing vasiculitis on the basis of a bacterial allergy
4. Nosological and clinical peculiarities of the so-called arteritis temporalis
5. The experimental endoangiitis and the influence of medication on it.
6. About the changes of vessels after typhus-paratyphus vaccination and in the case of endocarditis and aortitis fibroplastica, et cetera
7. About the signs of poisoning through penicillin
8. Allergization through penicillin
9. Dangers of novocain through novocain allergy
10. About the pathogenesis of accidents of chemotherapy and their therapy
11. Experimental investigations on the anaphylactoid reactions after artificial blood replacing substances.
12. Blood transfusions and allergy.

NEW RESIDENCY IN ALLERGY

Northwestern University Medical School offers a new residency in Allergy in connection with the new Veterans Administration Research Hospital. The Resident will be in charge of a service at the hospital and spend half of his time at the Medical School in clinics and research. This Residency is in addition to the Fellowship in Allergy which will be continued to be offered at Northwestern. The service will begin July 1, 1954. Applications should be made to Dr. Samuel M. Feinberg, 303 East Chicago Avenue, Chicago 11, Illinois.

PHILADELPHIA ALLERGY SOCIETY

The following are the newly elected officers for the year 1954, of the Philadelphia Allergy Society:

President—George W. Truitt, M.D.
Vice President—Charles S. Pennypacker, M.D.
Secretary-Treasurer—Edmund E. Ehrlich, M.D.

SWISS ALLERGY SOCIETY

The Swiss Allergy Society will meet May 20, 1954, in Zurich, Switzerland.

NEWS OF MEMBERS

Dr. Jack A. Rudolph announces that he is back in active practice at 1005 Kane Concourse, Bay Harbor Islands, Miami Beach, Florida.

BOOK REVIEWS

EXPERIMENTAL ALLERGIC REACTIONS INDUCED BY SIMPLE CHEMICAL COMPOUNDS. Mitsuteru Ishikawa, M.S., M.D., Professor of Tokyo Jikeikai School of Medicine, Tokyo, Japan. 122 pages. Tokyo: Maruzen Company, Ltd., 1953. Price $2.00.

This monograph represents twenty years of investigations on various aspects of experimental anaphylaxis with the aid of a research grant from the Ministry of Education. It contains the résumé of studies on the allergic reactions induced by simple chemical compounds and related phenomena conducted in the author's laboratory under his guidance or with his collaboration. The book describes the sensitizing capacity of forty-nine diverse chemicals and the sensitinogens, the mechanism of sensitization, allergic antibodies, manifestations of hypersensitivity to these chemical compounds, various aspects of the phenomenon, production of other antibodies demonstrable by test tube reaction, and capacity to induce Shwartzman phenomenon. There are 168 references to the literature cited. The book is very readable and should be of interest to all physicians interested in allergies.

PRACTICAL DERMATOLOGY. For Medical Students and General Practitioners. George M. Lewis, M.D., F.A.C.P.; Professor of Clinical Medicine (Dermatology) Cornell University Medical College; Attending Dermatologists, The New York Hospital; Secretary, the American Board of Dermatology and Syphilology, New York, N. Y. 328 pages, 99 figures. Price $7.50. Philadelphia and London: W. B. Saunders Company, 1952.

This is a concise and well-illustrated text for medical students and the practicing physician. It fills a demand for a text aimed at accurate diagnosis and identification of skin lesions commonly seen in the clinic and in the office. It will also serve as an aid in orientation for specialists. The author has admirably embraced all types of skin disorders in adults and children. There are twenty-five chapters and a suitable bibliography and index. There are ninety-nine plates of outstanding photographs of skin lesions taken by an expert. Points which the author wishes to emphasize are in heavy type. The symptoms, etiology, treatment, diet, local measures, ultra-violet-ray therapy, antibacterial remedies, antiseborrheic measurses, endocrine therapy, x-ray therapy and other remedies are given for each disease when indicated. Chapter 25 consists of a dermatologic formulary for reference when prescribing for any dermatologic lesion. Also, there is a formulary index for quick reference and lists of agents for patch testing. Allergy, when indicated, is given due consideration. The book should be a valuable adjunct to the student, general practitioner and specialist. The binding and format of the book are of the usual Saunders' high quality.

1954 MEDICAL PROGRESS. A Review of Medical Advances During 1953. Edited by Morris Fishbein, M.D., Clinical Assistant Professor of Medicine, University of Illinois College of Medicine, Chicago, Ill. 345 pages. New York and Toronto: The Blakiston Company, 1954. Price $5.00.

With the rapidly increasing and comprehensive literature in medicine, there is always need for an annual volume on progress in the various fields of medicine. This second volume appears to be better organized, although the first volume was an initial success. There are nineteen chapters on the various medical specialties and a summary of medical advances by the editor. All the authors are experts in their fields and reflect their ability when evaluating the importance of selected literature.

The chapter on allergy is again written by Leon Unger. The author very ably comments on, and briefly reviews, the past year's literature on allergy, its etiologic

factors, drug allergy, diagnosis and treatment of allergy, the role of infection, allergy of the nose and nasal sinuses, migraine, allergy in children, dermatologic allergy and miscellaneous allergies. There are 262 references on articles which appeared in 1952 and 1953 on the subject.

The editor summarizes, in Notes on Medical Advances, the most important advances for the past year. He reports on electrocortin, the new mineralocorticoid, the chief value of which lies in its probable ability to correct electrolyte abnormalities. The present status of antipoliomyelitis vaccine is clearly stated as well as the relation of hypertension and cholesterol. There are notes on cortisone and cancer, fatigue, eruption from detergents, destruction of Trichina larvae, gamma globulin and infectious jaundice, new drugs, smoking and cancer, costs of hospital care, as well as some miscellaneous notes. The book is well indexed and has a durable binding for rugged desk use. The general practitioner will find this review of particular value in keeping abreast of the current literature, and it also serves as a good reference for the specialist.

THE ALLERGIC CHILD. A Help and Guide to Parents. By Harry Swartz, M.D., New York, N. Y. 297 pages. New York: Coward-McCann, Inc., 1954. Price, $3.95.

The Allergic Child is a book directed solely to the layman. It is estimated that there are about five million children under fourteen years of age who suffer from one or more of the allergies. The purpose of the book is to show parents how to recognize the condition and to impress them with the necessity of early and prompt treatment. Also the author has evaluated the various methods of management of the allergic child, and brings to the attention of parents that allergies are found in normal children and not confined to the neurotic child. There is an important chapter on nutrition which stresses the fact that foods are important offenders and can be the cause of an allergy. There is also an appendix with a list of certain foods prepared for the allergic person and the composition of common foods. There are thirteen chapters covering the field, together with a glossary. Many books have been written for the laymen; however, this volume is sufficiently detailed to cover the subject excellently. It reflects also the opinion of a number of expert consultants. Although the book is originally designed for lay cosumption, it contains so much detailed information which the allergist or practitioner must know it will serve as a reference book. All physicians would do well to recommend this book to the parents of their allergic patients.

P-Q-R-S-T. A Guide to Electrocardiogram Interpretation. Third Edition. By Joseph E. F. Riseman, M.D., Clinical Associate in Medicine, Harvard Medical School; Instructor in Medicine, Tufts Medical School, Boston, Mass. 123 pages. New York: The Macmillan Company, 1952. Price $4.00.

This third edition guide booklet brings up-to-date interpretation of electrocardiograms. It is presented in an excellent compact form for ready reference not only for the student of cardiology but for the general practitioner and the specialist. The booklet is divided into two parts.

Part I consists of an Introduction presenting normal variations and directions for reading electrocardiograms. It presents the standard leads as well as the single apical precordial lead, the four lead ventricular patterns and unipolar and precordial leads.

Part II deals with physiological considerations and there are numerous case histories illustrating the various patterns, the technique of performing the test, together with an excellent glossary and a final table of cardiac rates.

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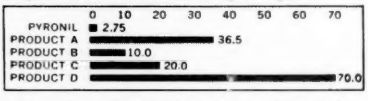
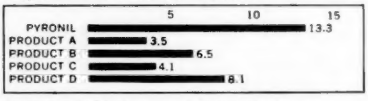


Maximum Duration of Effect in 50 Percent of Guinea Pigs Subjected to a Histamine Aerosol (Hours)*



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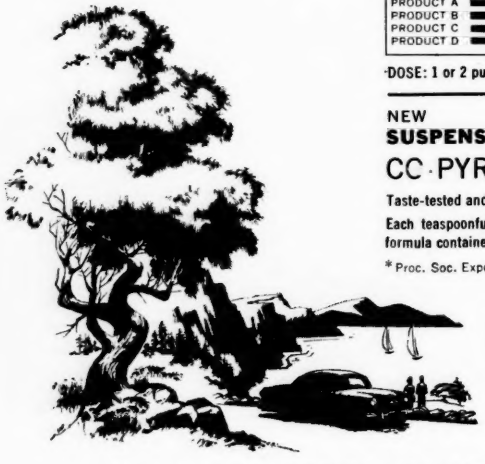
* Proc. Soc. Exper. Biol. & Med., 80:458, 1952.



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